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## EDITORIAL

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### THE DAWN OF A NEW ERA IN SCIENTIFIC PHARMACY.

The article published in this issue by Dr. Llewellys Barker on therapeutic measures; the papers read at the last meeting of the American Medical Association in the section devoted to Pharmacology and Therapeutics by Rountree, Young, Crile and others; the last presidential address of the British Pharmaceutical Association; the address of the President of the American Medical Association calling attention to a renewed interest in pharmacy and therapeutics; the examples of the close union of schools of pharmacy with hospitals in Germany and the efforts being made in this direction in this and other countries, are but evidences that a new era is at hand in the history of pharmacy and that its growth in usefulness and importance in the interests of humanity and medicine is so well advanced and determined that we can not afford to fail to respond to the inspiration of the great work planned by all thinking minds for the decade to follow.

The Philadelphia College of Pharmacy and Science, for the past one hundred years has been a leader in all that pertains to pharmacy and the allied sciences and the progressive element in the Board of Trustees, the Faculty and the College body appreciate fully the importance of the present movement and desire that this institution shall be among the foremost to join in the efforts to advance the interests of this great profession with all its varied interests and ramifications in both the professional and business world.

With this end in view, the efficiency of the College has been improved and enlarged, made possible by the financial assistance of the Board of Trustees and a few friends of the institution. The College has been renovated and repaired to try to provide proper,

adequate and comfortable quarters for its work and its faculty and curriculum expanded to meet the demands of the awakening interest in pharmacy and therapeutics. The allied branches of the work—general chemistry, industrial chemistry, physiological chemistry, bacteriology—have equally been provided for and at the same time measures have been taken to raise the general standard of educational pre-college work, which has already brought to the institution a class better equipped for the work than ever before. To supply a broad and thorough basic education as a preparation for our professional courses, instruction in the languages, in mathematics, and in business methods, has been provided, in order that the graduate shall go forth well equipped for work in the world and with a foundation that makes possible successful life work whether it be in pure pharmacy or its business branches, such as the retail drug business or the great manufacturing houses or in the work of pure research whether it be botany or chemistry or physiology or bacteriology. It will be the effort of the College to provide instruction in its regular and post-graduate work which will enable its students to successfully enter the fields of life work in the many splendid openings existing today as real pharmacists, as analytic chemists, as directors of great sanitation problems, as research workers either independently or in the great laboratories of our educational and industrial institutions, to be directors and assistants in the bacteriological and biological laboratories of educational institutions, of general and municipal governments, in the great drug manufacturing laboratories, to carry on work of this kind in pharmacies and drug stores which maintain laboratories great or small and to be the skilled assistants of physicians in those important branches of their practice involving all that pertains to the chemical, bacteriological, biological examinations of their patients and which the physician has not the time and often not the technical skill to perform.

A glance shows the vast importance, the numerous splendid openings for the work contemplated by the present organization of the College. It must not be overlooked also that the pre-professional work to be obtained in this College provides the best possible basis for those who intend ultimately to study and practice medicine. In fact it must be apparent that no medical man can hope to enter on his profession, equipped for research and scientific medical attainment without the basal information given in the work of this school.

The fact that medicine and pharmacy have grown apart during

the past years is regretted by both professions and their closer union is absolutely necessary for the success of each in its humanitarian work.

The great need of the present day as Dr. Rountree states at the close of his address before the Section on Pharmacology and Therapeutics of the American Medical Association is the establishment of a "National Institute of Pharmacology and Experimental Therapeutics."

This idea has been in the minds of some of the trustees and officers of the College and it has been thought that a movement along this line might be contemplated with the College of Pharmacy and Science of Philadelphia as a center, linking up its work with a great hospital existing or to be built in the city in connection with a manufacturing plant under the control and direction of the College, with an adequate animal farm for biological products and an extensive botanical and research garden for the systematic study, cultivation and standardization of therapeutic drug plants.

This would allow the equal and co-ordinate union of the College for teaching, research and standardizing all that pertains to pharmacy and its allied branches in chemistry and bacteriology, the proper preparation for safe and scientific administration of its products and the determination of their value at the bedside in the associated hospital by the best staff of attending and consulting physicians the city could produce. This would bring about, ideally, the union of the doctor, the scientific pharmacist and the highest and best method of making the therapeutic agent for human use. As a co-ordinate body they would work constantly together and the final approved therapeutic agent, with its full history, characteristics, mode of application and method of manufacture would then be given to the world for its use and to the commercial manufacturers for production. No commercial element enters into this proposed organization. For this purpose a sufficient endowment must be raised to place the College, the hospital, the manufacturing plant absolutely outside of any possible commercial implication. If possible the patients at the hospital should be free patients, but given the best of every hospital attention and equipment. Philadelphia, which needs so acutely, larger facilities for the care of its sick, could well assist to make so magnificent a contribution to the welfare of its population and indirectly to that of the world.

This outline of the visions of the possibilities of the future it is

hoped will stimulate thought and action in the forward movement of the work and help lead to the assistance and solution of the great problem before us.

The College possesses already on its staff men of splendid attainment and untiring energy and courage to prosecute its work. Never have I seen a group of educators better equipped to inspire the young, to give instruction that has real, practical, useable worth in the life work. With the increase in the faculty more time will be given for problems of research, which in the past has been so important, inspiring and valuable. It is hoped when the reorganization is complete that the resources of the College may be made available to the outside world in order that its problems may be referred to our research workers for solution and if this work can be provided practically free of charge, many a splendid idea may result in practical fulfillment and use.

In view of the splendid possibilities can there be one among us who will not do his utmost to see that at last pharmacy may be given its fair chance to develop itself in the world's work?

W. C. B.

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## SELECTED EDITORIAL

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### THE LIVE WIRE MIND.

When a mentality like Edison's sets questions, such as have been widely discussed and criticized, it behooves more commonplace minds to "stop, look and listen." Mr. Edison, quite unintentionally, has stirred the educational world and, as in all such stimulations of the gray matter, we find ourselves getting "back to the Greeks," the source of all philosophical thinking and initiative. The mind of an inventor is an inquiring one: he is not content to tread the old beaten paths around, but tackles, directly, the obstacles in front. To do this, observation of all sorts and conditions of things keeps the mind supple and alert. Some of these queer shaped and unimportant bits of knowledge may be found to fit into these other equally odd shapes and, little by little, his picture puzzle reveals a perfect whole. Who would have supposed that the study of the anatomy of the mosquito would reveal the true source of malarial fever, and that by this knowledge vast areas of the earth would be reclaimed for

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habitation? When Joseph Leidy noticed and questioned what might be the white specks in the ham served for his luncheon, his mind opened the way to the discovery of the parasite disease in pork, against the eating of which, as told in the Book of Leviticus, the Jews had blindly enacted laws centuries before. The large majority of us are of the cog and ball-bearing type of mind. Specialization today is begun so early that the foundations of knowledge and philosophical thinking are very narrow. The question of moment to American educators is whether our schools and colleges are developing the greatest number of observers possible, or whether the ordinary student is constrained to tread the beaten paths with never a look to right or left and never an impulse to inquire into the mysteries that lie near by. The man of the bush who first used ash or hickory for his axe handle was a greater observer than the college man who thought cork came from Ireland. A man with an inquiring mind is what Edison calls a "live wire," interesting and interested; and in no way does this interfere with his being a highly specialized technical expert in any line he may be engaged in. Is our system of education making for or against this mind development? It is not whether a man can answer correctly all these questions, but whether he is asking these and similar questions of himself when he meets them in his daily reading and conversation. It was mind exercise and not mere knowledge that enabled the Greeks to initiate, in physics, geometry, literature, art and on through a long list, the foundations on which we build today. So, "back to the Greeks," who taught us observation, general and specific, with philosophical deductions. Concentration has its advantages; but unless the object is held at sufficient distance, the observer looks cross-eyed and loses his sense of proportion.—(*Jour. of the A. M. A.*, Aug., 1921.)

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## ORIGINAL PAPERS

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### THE CHEMICAL ELEMENTS OF LIVING MATTER.

By INGO W. D. HACKH,

COLLEGE OF PHYSICIANS AND SURGEONS, SAN FRANCISCO.

It is a remarkable fact that relatively small number of elements enter into the composition of living matter, whether of vegetable or animal nature. Naturally the elements, excepting oxygen, enter the

metabolism of the cell organism, not as free elements, but as compounds. These compounds we speak properly of as *food*, of which there are the four great classes of proteins, carbohydrates, fats, and salts. The first three classes all contain hydrogen, carbon, oxygen, and sometimes nitrogen. These four elements are of paramount importance in all life processes, and the multitude of compounds, which they are able to form, is the main study of biochemistry. To indicate the service of these elements in the living organism is the aim of this article, although present knowledge is far from complete. The importance of the elements is shown in the three groups:

- a. The true life elements or bioelements which are invariably present in all vegetable or animal matter;
- b. Elements which commonly occur in cell organism, and which seem to be characteristic of certain tissues;
- c. Elements occurring rarely in the living organisms, which seem to be more or less adventitious.

#### THE TRUE LIFE ELEMENTS OF BIOELEMENTS.

i. *Carbon*, well known as the structural element which gives to the large number of organic compounds their complexity of form and function, is the corner-stone of organic cell metabolism. Its valency of four is significant, as it explains the fact that an atom of carbon has to another carbon atom a greater affinity than to an atom of another element. In other words the attractive power of a carbon atom is greatest<sup>1</sup> to another carbon atom for its electromotive force is nearly zero, it can act therefore sometimes as positive, sometimes as negative atom and produces the many chains and rings of organic compounds. According to the latest theories of chemistry, the stable compounds all contain eight or a multiple of eight valence electrons, these alone forming a stable system.<sup>2</sup> Carbon, having four valence electrons, combines therefore readily with other carbon atoms to an octet or stable system of eight electrons.<sup>3</sup> The recognition of this ability of the carbon atom will explain its pre-

<sup>1</sup> Geoffrey Martin, Ueber das Affinitätsgesetz im Per. Syst., Inaug. Diss., Kiel, 1906; page 23.

<sup>2</sup> Lewis's theory of cubical atom, Parson's theory of magneton, Langmuir's octet theory and others.

<sup>3</sup> E. g., sodium has 1 free valence electron, chlorine has 7, thus NaCl has together 8 valence electrons. Hydrogen has 1, in CH<sub>4</sub> there are thus 8, in C<sub>2</sub>H<sub>6</sub> 16 or (2x8) valence electrons.

dominant function as the substance endowing complexity, variability and individuality to organic compounds.

2. *Hydrogen*, constituent of water and present in all acids and bases, plays an important role in biochemical reactions. Free hydrogen gas, a mild reducing agent, is formed as fermentation product and occurs in the intestinal gases of mammals, the result of bacterial composition of the carbohydrates:

*Composition of Intestinal Gases (Ruge)*

<i>100 volumes contain</i>	<i>H<sub>2</sub></i>	<i>N<sub>2</sub></i>	<i>CO<sub>2</sub></i>	<i>CH<sub>4</sub></i>
in vegetable diet	1-4	10-19	21-34	44-55
in meat diet	1-3	45-64	8-13	26-37
in milk diet	43-54	36-38	9-16	1-2

Many biochemical reactions are due to the formation of water or neutralization  $H + OH = H_2O$ . Free acids or  $H+$  (hydrogen ions) are of importance in gastric digestion and animal respiration. Bases or hydroxyl ions ( $OH^-$ ) occur in the saliva and other secretions. The splitting off of water takes the place in the synthesis of carbohydrates while the taking up of water occurs in the hydrolysis or breaking down of the carbohydrates. To the great affinity of hydrogen for oxygen, many other reactions must be ascribed which involve the dissociation and separation of oxygen from various compounds. Hydrogen, therefore, is the active principle in the cell metabolism which is readily oxidized, and performs the service of a reducing agent.

3. *Oxygen*, the great oxidizer, circulates in the cell-organism as the releaser of energy,—it is the energy carrier of life furnishing heat and power to the living machines. Both hydrogen and oxygen are, as water, the principal constituent of protoplasm,—without water there could be no cell-life. But free oxygen is the great sustainer of life, it is absorbed by the blood of animals, and carried to every cell in need of it, yielding by its reactivity heat and energy.

*Composition of the Gases of Blood*

<i>100 vol. blood contain</i>	<i>O<sub>2</sub></i>	<i>N<sub>2</sub></i>	<i>CO<sub>2</sub></i>
of arterial blood	18	2	40
of venous blood	12	2	48

Oxygen is not only the most abundant, but also the most important element and its discovery laid the foundation of modern chemistry.

To the cell metabolism oxygen is the element which burns up the waste-products and oxidizes food materials thereby liberating the stored energy in the form of heat.

4. *Nitrogen*, the apparent inert and lazy gas of the atmosphere, is the element giving instability and therefore reactivity to organic compounds. Nitrogen can form several series of compounds which are more or less readily transformed into each other. Thus there are the compounds of the lowest valence number (-3) or compounds derived from ammonium ( $\text{NH}_3$ ), to this class belong the amino acids ( $\text{NH}_2\text{-R-COOH}$ ) which are the bricks or building stones of the proteins. The next series of compounds are derived from nitrous oxide ( $\text{N}_2\text{O}_3$ ) with a valence number of +3 and in this series there are the nitrites, which are readily oxidized to nitrates. Finally the compounds derived from nitric oxide ( $\text{N}_2\text{O}_5$ ) form the nitrates (valence number +5) and are the highest stage of oxidation. Nitrates are important as fertilizers from which the plant synthesises the complex proteins by reducing processes. Nitrogen forms with C, H, and O a number of important radicals and compounds, its rôle in the cell-metabolism seems to be the imparting of instability and sensitiveness to protoplasmic compounds.

5. *Phosphorus*, the controlling element, is indispensable to the nucleus of the cell. It occurs in nucleins, lecithins, and vitellins; is essential for nerve and brain cells of animals, and accumulates in seeds and buds of plants. It is a constituent of chromatin, the intranuclear germ plasm, which is supposed to be the seat of heredity.<sup>4</sup> It is essential in the assimilation of fats which are transformed into lecithins before assimilation and seems to accumulate in those parts of the cell-organism where the important function of cell-division is performed:

*Content of  $\text{P}_2\text{O}_5$  in the Ash of Plants:  
100 parts of plant ash contain  $\text{P}_2\text{O}_5$*

in roots average	12-17%
in stems "	4-12%
in leaves "	9-13%
in seeds "	37-49%

<sup>4</sup> Osborn, *Origin and Evolution of Life*; N. Y., 1917; page 21 ff.

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In ionized form, as phosphates of sodium and potassium, it maintains the neutral reaction of blood and other liquid tissues (buffer solution). The solid phosphates of calcium and magnesium are predominant in the skeletons of animals. Small doses of phosphorus stimulate the brain and circulation, the function of the genital organs, and the growth of bones. Phosphorus is thus the regulating and controlling element of the cell metabolism.

6. *Sulfur*, as essential constituent of the proteins, is invariably present in animal and vegetable organisms. It is a constituent of the aminoacid cystin and so occurs in keratin or the epidermal protein, in connective tissues, in taurocholic acid of the bile, and as sulfates in blood and other liquors. Free sulfur occurs in the protoplasm of certain protozoa or unicellular animals. Hydrogen sulfide is a constituent of the intestinal gases of vertebrates, formed together with mercaptans from the decomposition of proteins rich in cystin. Sulfocyanates occur in saliva, nose secretions, and urine, while sulfuric acid has been found in the saliva of certain snails as the product of bacterial metabolism. The ash of plants contains on an average from 0.7—7% of  $\text{SO}_3$ .

7. *Magnesium*, present throughout the cell organism, occurs especially as magnesium phosphate in bones, teeth, blood, muscles and nerves of the vertebrates. It is abundant in many lower animals (*e. g.*, corallinaceae). As permanent constituent of chlorophyll it is essential to the metabolism of plants. Aetiophyllin  $\text{C}_{31}\text{H}_{34}\text{N}_4\text{Mg}$ , a constituent of chlorophyll, is a substance closely related to haemophyllin of the haemoglobin of blood. Magnesium has a close relation to phosphorus, for it is more abundant in the plant parts undergoing development (seeds and growing tips) and is absent in maturing organs. Oily seeds contain more Mg than starchy seeds,—by the absence of Mg no oil is formed. It is a vehicle for the assimilation of phosphoric acid and so aids indirectly the formation of nucleoproteins.

*Content of  $\text{MgO}$  in the Ash of Plants:*  
*100 parts of plant ash contain  $\text{MgO}$*

in roots, average	3-7%
in stems, average	2-4%
in leaves, average	4-12%
in seeds, average	8-17%

8. *Iron*, the respiratory metal of animals, is present in all protoplasm and is essential to the formation of coloring matter (chlorophyll of plants, haemoglobin of animals). In haemoglobin it serves higher animals as an oxygen carrier (1 gm. Fe to 150 gm. of red blood corpuscles). The human body contains about .005% iron, it occurs in bile, lymph, chyle, gastric juice, pigment of eye, milk and in urine. Its most important function is its presence in haematin  $C_{34}H_{84}N_1FeO_5$  of the haemoglobin which acts as transmitter of oxygen from the lungs to the tissues, and of carbon dioxide from the tissues to the lung (respiration). It is also invariably present in the vegetable organism:

*Content of  $Fe_2O_3$  in the Ash of Plants:*

<i>100 parts of ash contain</i>	$Fe_2O_3$
in roots, average	0.8-2%
in stems, average	0.6-4%
in leaves, average	0.5-1%
in seeds, average	0.5-2%

Lack of iron leads to pathological chlorosis; in plants the leaves do not seem able to form chlorophyll, become pale and unable to photo-synthesis.

9. *Potassium*, the most electropositive metal, is essential to the living tissues of plants and animals. It occurs in two forms: (a) ionized as chlorides, phosphates, sulphates and carbonates, and (b) masked in organic combination as constituent of a large molecule. In the regulation of life processes the potassium salts play an important rôle as stimulating agents, acting on the brain, vaso-motoric and sensory nerves of animals. In the plant organism it is important in the formation of carbohydrates and proteins, for without K no starch is formed. Seeds and other organs rich in proteins are usually rich in potassium:

*Comparison of Protein and Potassium:*

<i>100 parts contain</i>	<i>Protein substance. of dried</i>	<i>of ash.. Potassium</i>
Seeds of cereals, average	10.2%	23.07%
Seeds of legumes, average	29.0%	39.2%

Content of  $K_2O$  in the Ash of Plants:

100 parts of ash contain	$K_2O$
in roots, average	45-60%
in stems, average	13-47%
in seeds, average	23-42%
in leaves, average	26-36%

Certain fresh water and marine plants are able to store large quantities of potash, *e. g.*, the Pacific Coast Kelps (*Phaeophyceae*). A small percentage can be substituted by the other alkali metals. Potassium occurs mainly in the cell-membranes and tissues and seems to act as osmotic agent. The saps and juices sometimes contain K which may be replaced by sodium.

## ELEMENTS WHICH COMMONLY OCCUR IN CELL ORGANISM.

10. *Fluorine* is found in small amounts in bones (0.05-0.2% of ash), teeth (0.18% of ash), brain matter (0.8 mg. in 100 gm.), cow's milk (0.3 mg. in 1 liter), egg-yolk (1.1 mg. in 100 gm.). It occurs also in blood where it seems to play a protective and regulatory part in the process of coagulation of fibrin. It is also found in certain mollusks and many plants.

11. *Chlorine* because of its abundance in sea-water is present in marine algae and many other plants, though it seems to be not essential for the complete development of higher plants. It is essential to animals, occurring mainly as NaCl in blood, lymph, tears, sweat, and urine. As free HCl of the gastric juice, it takes part in the digestion of food. The percentage of Chlorine in different tissues is

blood	0.268%	spleen	0.107%	bonemarrow	0.034%
lungs	0.150%	brain	.100%	muscles	.033%
skin	0.145%	stomach	.093%	liver	.025%
kidney	.122%	intestine	.040%	bile	.010%

12. *Bromine* occurs in traces in all organs of mammals. It is abundant in marine algae, but little is known of its function.

13. *Iodine* is essential to vertebrates as a constituent of iodo-thyrin of the thyroid gland. The amount of I in the gland is variable from 0.077-3.85 mg. of iodine per 1 gm. of the dry substance

of the gland (fresh weight of gland in adults 29 to 231 gm., dry substance from 5 to 62 gm.) Iodine occurs in star fishes from 0.007-0.24%, in sponges 1.5% (as iodospongin  $C_{56}H_{87}IN_{10}-S_2O_2$ ), in oysters, sea weed, and especially brown algae, while the corals, *Gorgonia Carolinii*, may contain from 0.7-7.8% of I. Besides in the thyroid gland iodine is reported in the following organs and tissues of man:

liver 1.214 mg. I in 100 gm.	skin and hairs	0.88 mg. I
kidney 1.053	blood, menstrual	0.09 "
stomach .909	" normal	0.021 "

14. *Silicon* is always present in small amounts in vertebrates, mainly as a constituent of the teeth and bones:

*1000 grams of dry substance contain*

enamel of teeth	0.581 gm. $SiO_2$	tendons	0.064
Wharton's jelly	0.243 " " skin		0.044
dura mater	0.087 " " muscles		0.024

It is also present in radiolarians and siliceous sponges and is found in all plants, predominant in the stems of many grasses, in diatoms and in marine algae. Cereal straws and corn stover may contain 40-70%,  $SiO_2$  equisetaceæ 70-80%  $SiO_2$  of their ash. It appears to be chiefly in the cell wall and to act as support and protective substance.

*Content of  $SiO_2$  in the Ash of Plants:*

*100 parts of ash contain  $SiO_2$*

in root, average	1-3%
in stems, average	6-70%
in leaves, average	5-40%
in seeds, average	0.5-3%

15. *Sodium* is essential for animals but not plants. It is abundant in blood and lymph and also occurs in many plant saps and juices. In muscles (5-6%), brain (1½-2%), and liver (2%) there is more K than Na, while the proportion of K:Na is equal in heart and kidney, but in the pancreas (1-4-1-3%), spleen (5%), and bones (6%) there is more Na than K; and cartilage contains only sodium. Like K it has an osmotic function.

*Content of Na<sub>2</sub>O in the Ash of Plants:*

100 parts of ash contain Na <sub>2</sub> O	
in roots, average	2-10%
in stems, average	1-4%
in leaves, average	0.8-2%
in seeds, average	0.6-2%

16. *Calcium* is widely distributed in animals and plants and is important in regulating biochemical reactions through irritability and stimulation; *e. g.*, in vertebrates the clotting of blood, in plants the protein formation of calcium proteids, nucleo-proteins, and plastides of cell. In vertebrates the skeletal material is chiefly calcium phosphate, in invertebrates calcium carbonate. There are in

muscles	.005% CaO	pancreas	0.15% CaO
blood	.006%	lungs	.016%
brain	.009%	liver	.029%
kidney	.009%	heart	.025%

In the plant organism it accumulates in leaves and vegetative organs and there appears to be a relation between the Ca content and carbohydrate digestion.

*Content of CaO in the Ash of Plants:*

## 100 parts of ash contain CaO

in roots	2-11%
in stems	5-25%
in leaves	6-32%
in seeds	2-9%

17. *Manganese* always appears in traces in animals and plants. It is found not only in blood (0.5-2.5 mg. per liter), milk bones, hairs, tissues of mammals, but also in the ash of plants. Manganese salts have recently been considered as fertilizer for plants,<sup>5</sup> but their rôle in the metabolism is little understood. They seem to act as stimulants and irritants by regulating the motor activities of the cell organism. The large amount of Mn in the ash of the pancreas (2.2-2.5%) is remarkable.

18. *Aluminum* is abundant in soil and therefore widely distributed in plants. Cryptogams contain Al mainly in their stems, while angiosperms have much Al in their blossoms and flowers. Pine needles are especially rich in aluminum.

\* U. S. Dept. Agricult., Bull. 600, 1917.

## ELEMENTS OCCURRING RARELY IN LIVING ORGANISMS.

19. *Lithium* occurs, in traces, apparently in all animals and plants and seems to be a constant constituent resembling the other alkali metals in its function. The lungs of mammals contain lithium salts. Lithium compounds are rapidly absorbed and eliminated by the kidneys—no case of poisoning has so far been recorded.

20. *Rubidium* is found in various animals and plants.

21. *Cæsium* occurs in traces in some animal organs and in many plants (timothy, raspberry, beets, etc.).

22. *Strontium* is present in animals and plants in variable amounts and seems to be of accidental occurrence.

23. *Barium* is found in some plants grown on soil containing barytes.

24. *Radium* occurs in minute traces in animals and plants.

25. *Boron* is sometimes found in the ashes of plants, especially if grown on soil rich in tourmalin and its decomposton products (Belgium, So. California).

26. *Zinc* has been reported in the human liver (10-76 mg. per kg.) ; traces are also found in corals and some plants.

27. *Copper*, while not essential for vertebrates, occurs in the human body; especially in the blood, brain, kidney (1.2-2 mg. per kg.), spleen (3.2-5.6 mg. per kg.), liver (1.5-15 mg. per kg.). It is essential for invertebrates where it plays the same rôle which iron does in vertebrates, namely as respiratory metal and oxygen carrier in the form of haemocyanin. The bluish blood of molluscs (Cephalopoda and Gastropoda) contain large amounts of copper (e. g., oysters, octopus, lobsters, helix pomatia, Limulus cycleps and Sabella species). It has also been found in the plumage of a bird, the turaco or Cape Lory, whose red feathers contain turacin (7% Co.).

28. *Nickel* and 29. *Cobalt* occur in traces in some plants.

30. *Chromium* is occasionally found in small amounts in some plants.

31. *Vanadium* is exceedingly rare, found only in few cases.

32. *Titanium* is found in slight traces in nearly all plants and appears to be a constant constituent like silicon.

33. *Cerium* occurs in traces in some plants. As oxalate it has been found in bones (0.03 gm. Cerium oxalate in 1 kg.).

34. *Tin* and 35. *Lead* have been found in some organs. Human kidney, liver, hairs, and nails contain traces of lead; some corals contain small amounts of lead.

36. *Arsenic* occurs in some animals and many human organs. In chronic arsenic poisoning the amount of As in the skin is increased considerably, often causing a brown pigmentation of the skin, probably due to the formation of sulfides. (Keratin contains S.) The minute traces of arsenic in human organs are:

skin	.0026 mg.	As in 100 gm.	liver	.0019 mg.	As in 100 gm.
pancreas	.0029 mg.		kidney	.0015 mg.	
hairs	.0049 mg.		brain	.0013 mg.	

Elements found in isolated cases in animals and plants are: Geranium, thallium, mercury, solenium, silver.

No other elements have been reported to enter into cell organism.

Summarizing the occurrence of elements in living organisms, vegetable or animal, only four elements form its bulk, namely 97-99% of which O = 52-63%, C = 20-38%, H = 7-10% and N = 0.03-3%. The lowest plants have in addition S, K, and Ca,—while the chlorophyll-containing plants also contain P, Mg, and Fe,—in animals Cl, Na, Si, and I are necessary. It appears that with complexity of functions the number of elements taking part in cell metabolism increases; hence the more highly developed an organism, the greater the number of elements which enter into its composition and which are thus usually present in some highly specialized organ; as *e. g.*, iodine in the thyroid glands.

Considering the living organism as a chemical machine consisting of protoplasmic units or cells, it appears that the essential elements function in two ways: (a) As component parts of the cell structure; *e. g.*, S in the cell wall and the epithelial tissue, P in the nucleus, Si in the stem of certain plants, Ca in the skeleton of animals and the stems of plants; and (b) as agents causing physical or chemical reactions; *e. g.*, the respiratory metals Fe (vertebrate blood), Mn, Cu (invertebrate blood), K in the root of plants, Mg in seeds and leaves.

Many of these elements are associated and occur in pairs, thus in the vegetable metabolism Mg and K are predominant, while the corresponding pair in the animal organism is Fe and Na. These two pairs are also found in igneous rocks.<sup>6</sup> Again there is an accumulation of certain elements in definite tissues of the organism, thus in the vegetable organism the seeds are rich in P and Mg and depleted of Ca and K, while the stems and leaves contain much Ca, K, and often Si, and the roots are rich in K and depleted of P.

The specific rôle of the elements is little understood and so it is speculative to account for their presence. It seems that the presence of an element, other than the 9 or 12 essential ones, is the result of either evolution or adaptation. Thus the occurrence of iodine in the thyroid gland of vertebrates seems the result of evolution; *e. g.*, the utilization in a highly specialized organ of the organism, while its presence in marine plants and invertebrates seems the result of adaptation, *e. g.*, diffused throughout the cell organism with apparently no distinct function. Likewise the presence of copper in the blood of certain invertebrates seems due to evolution, while its presence in bacteria, grown successively for several generations upon a copper containing culture media, is adaptation.

An interesting comparison of the distribution of elements in living organisms and inanimate nature with its relation to the periodic system has been pointed out in previous papers<sup>7</sup> where it was shown that the elements of low atomic weights essential and occurring in living matter, cluster together in the periodic table and seem to point to an evolution. There are many unsolved questions in this fascinating problem. Why did the cell substitute in specialized tissues the elements of higher atomic weight for those of lower atomic weight, *e. g.*, Br and I for Cl and F? Is the answer merely to be found in physico-chemical phenomena, or has that mysterious controlling force guarding the entrance to the protoplasm exerted a selective process for a certain end? Is this force, the vital force, possessed of intelligence and not of a purely physical or chemical nature?

<sup>6</sup>H. S. Washington, *Sci. Am. Suppl.*, Vol. 83, page 27, 1917.

<sup>7</sup>*Journal of General Physiology*, Vol. 1, page 429, 1919, and *Science Progress*, Vol. 14, page 602, 1920.

## CONCERNING THE THERAPEUTIC ACTION OF SOME DERIVATIVES OF COD LIVER OIL.\*

By OSCAR BERGHAUSEN, B. A., M. D., and LOUIS A. STEINKOENIG,  
Ch. E., Cincinnati, Ohio.

### HISTORICAL.

The fatty oils have had a wide therapeutic application especially in the treatment of leprosy. Chaulmoogra oil derived from the seeds of Taraktogenos kurzii, was used for many years at the Molokai Settlement, and previous to 1865 by physicians in India in the treatment of leprosy. An excellent historical review of the chaulmoogra oil treatment of leprosy was published by George W. McCoy.<sup>1</sup> Power and his collaborators<sup>2</sup> discovered a new series of fatty acids represented by two members—chaulmoogric acid,  $C_{18}H_{32}O_2$ , and hydnocarpic acid,  $C_{16}H_{24}O_2$ , which they prepared from chaulmoogra oil.

The report of Dr. Victor G. Heiser<sup>3</sup> caused renewed interest in this mode of therapy and seemed to show that there were one or more active principles which had a specific action in leprosy and that this agent was more effective when given hypodermically or intramuscularly than when taken by mouth. Sir Leonard Rogers used the sodium salts of acids derived from chaulmoogra oil, using the fractions separated by Ghosh.<sup>4</sup>

In a more recent publication Sir Leonard Rogers<sup>5</sup> describes the use of gynocardate of soda and morrhuate of soda, the latter referring to the sodium soap of the fatty acids prepared from cod liver oil. Rogers suggests that "other unsaturated fatty acids may also be expected to yield effective preparations against the acid-fast bacilli of both leprosy and tuberculosis." McDonald and Dean<sup>6</sup> later published results using distilled esters of the fatty acids of chaulmoogra oil.

### SODIUM MORRHUATE.

Becoming interested in this subject we determined to study the therapeutic value of sodium morrhuate and the hitherto undescribed mercury salts of morrhuate acid. A. Gautier and L. Mourguet<sup>7</sup> ex-

\*Read before the Daniel Drake Society, Cincinnati, Ohio, June, 1921.

tracted cod liver with acidified alcohol and refined the extract, isolating finally a yellow oil which crystallized in the form of plates. They called this substance morrhuiac acid  $C_9H_{13}NO_3$ , assigning to it the structural formula of hydroxidihydropyridine-butrylic acid.

Sodium morrhuate can readily be used in the form of a 3 per cent. aqueous solution as suggested by Sir Leonard Rogers. If a sediment forms the supernatant solution can be used. This keeps at room temperature if 0.25-0.50 per cent. carbolic acid is added. It has a reddish brown color and a distinct odor of cod liver oil, and represents the sodium salts of mixed, unsaturated fatty acids.

Deep muscular injections of from one to four cubic centimeters have been given. The patient complains of some local tenderness lasting for a day or two, but these reactions are never severe. Intravenous injections are well tolerated, larger amounts causing a slight headache and a feeling of dullness, but general reactions in the form of chills and fever have not occurred. We have not noticed any evidences of phlebitis in the vessels selected for injections. It has been suggested that sodium morrhuate given intravenously could possibly lead to a stimulation of the immunologic mechanism concerned in the healing of infectious processes non-tubercular in nature. A limited experience in this field has failed to verify these predictions. We have not as yet tried out this new remedy in a series of patients suffering from pulmonary tuberculosis.

#### CALCIUM MORRHUATE.

By adding calcium acetate to a solution of sodium morrhuate containing  $1\frac{1}{2}$  per cent. gelatin and  $\frac{1}{4}$  per cent. carbolic acid, a suspension of calcium morrhuate was obtained. One c. c. of this suspension contained  $\frac{1}{6}$  grain of calcium morrhuate and  $\frac{1}{70}$  grain of gelatin;  $\frac{1}{2}$  per cent. aqueous formaldehyde solution can be used as a preservative. When these insoluble suspensions were given intramuscularly some local tenderness developed but no general symptoms.

#### MERCURIOUS MORRHUATE.

The mercurious preparation was found to be greyish in color, homogeneous, gelatinous and sticky in nature, and suitable for intramuscular medication in patients suffering from syphilis. It

was prepared by adding a newly made aqueous solution of mercurous nitrate to a 3 per cent. solution of sodium morrhuate to complete precipitation, washing and drying the precipitate in a current of warm air. Collapsules \* containing 3 grains of mercurous morrhuate, representing 50 per cent., *i. e.*, 1½ grains of metallic mercury were made at our request, by two prominent capsulating houses. Many of these capsule injections were made and have been found to be very satisfactory. The contents can readily be expressed from the collapsules without preliminary warning. (The amount of local reaction produced about equals that obtained with the ordinary two grain "salicidol" preparations.) Patients have not complained of the severe local reactions so common with the ordinary preparations heretofore employed.

#### MERCURIC MORRHUATE.

Mercuric morrhuate was obtained by adding a warm dilute solution of mercuric chloride to a warm dilute solution of an equivalent amount of sodium morrhuate, slowly and with thorough agitation. A reddish yellow, opalescent colloidal solution resulted. When an attempt was made to remove the sodium chloride and uncombined mercuric chloride by dialysis, the colloidal solution of mercuric morrhuate agglomerated. For this reason a more suitable preparation for intravenous medication was obtained by carefully calculating the amount of mercuric chloride required and making the suspension neutral to phenolphthalein by using a small quantity of dilute potassium hydroxide. This kept perfectly at room temperature only a slight precipitation taking place on standing.

It was found that syphilitic patients could tolerate as much as 3 c. c. of this suspension intravenously, without producing general manifestations. In one young girl of eighteen years, suffering from congenital syphilis, temporary symptoms vascular in origin developed after giving about 2 c. c. intravenously. When this preparation was added drop by drop to ordinary clear human serum, no precipitation of protein occurred. When added to freshly drawn blood in

\*Mr. L. W. Cyrenius, of the American Collapsule Company and Dr. Sheridan Baketel, of the H. A. Metz Company, were kind enough to prepare these collapsules, using the same medium as employed in the preparation of "salicidol."

the proportion of 0.5 c. c. to 2 c. c. of human blood and allowed to stand for ten minutes, no clumping occurred, and when centrifuged the supernatant plasma showed the merest trace of hemolysis. These results would indicate that the mercuric suspension is probably safe for intravenous medication.

#### LITERATURE.

<sup>1</sup> Studies upon Leprosy, xxviii, per *Public Health Bulletin* No. 175, January, 1916, pages 3-11, Government Printing Office, by Geo. W. McCoy and Harry T. Hollmann.

<sup>2</sup> Power and Gornall, the Constituents of Chaulmoogra Seeds. *Journ. Chem. Soc.*, lxxxv, page 838, 1904.

<sup>3</sup> *Public Health Reports*, Vol. 29, No. 22, page 2763.

<sup>4</sup> Sudhamoy Ghosh, Report of a Chemical Investigation of Chaulmoogra Oil in Connection with Leprosy Treatments. *Indian Journal Medical Research*, IV, page 691 (1916).

<sup>5</sup> Paper read before the Medical Section of the Asiatic Society of Bengal, March 12, 1919, by Sir Leonard Rogers.

<sup>6</sup> The Treatment of Leprosy. Reprint No. 607, from *The Public Health Reports*, August 20, 1920, pages 1959-1974.

<sup>7</sup> *Compt. Rend.*, 1888, 107, 740.

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## ABSTRACTED AND REPRINTED ARTICLES

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### THE VALUE OF DRUGS IN INTERNAL MEDICINE.\*

By LEWELLYS F. BARKER, M. D., Baltimore.

We are now witnessing a cautious revival of the use of drugs in the treatment of disease. During the last half of the nineteenth century pharmacotherapy fell more or less into discredit, owing (1) to a reaction against the scandalous abuse of the "shotgun prescription," (2) to the general therapeutic nihilism that followed the rise of studies in pathologic anatomy, and (3) to the growing recognition of the importance of forms of therapy other than treatment by drugs. Though in some quarters the denial of pharmacotherapy was pushed to extremes, it is now generally admitted that the move-

\*Read before the Section on Pharmacology and Therapeutics at the Seventy-Second Annual Session of the American Medical Association, Boston, June 21, 1921. Reprinted from *Jour. Amer. Med. Assoc.*, October 8, 1921.

ment against the indiscriminate and noncritical use of drugs, to the relative exclusion of other and often more efficacious methods of therapeutic intervention, was necessary and timely, in order that the more rational therapy of our period might emerge.

In the therapy of today, based on more accurate diagnosis and on enlarged conceptions of pathologic physiology, etiology and pathogenesis, a new hopefulness prevails. We make use now of a host of methods that are found to be trustworthy for healing, for palliating and for preventing. Along with diet, baths, climate, air, light, heat, exercise, massage, electricity, roentgen rays, radium, serums, vaccines, mechanical appliances, surgery, nursing, and psychic and social influences, drugs are gradually finding their proper place in the therapeutic armamentarium of the medical practitioner. For among the drugs of various sorts, including both natural substances and pure chemicals provided by separation or by synthesis, there are agents that can now be employed with great confidence and often with the happiest results.

#### DUTY OF THE INTERNIST.

In the management of patients and in the treatment of their diseases, it is our duty as physicians to see to it that we do not neglect to make application of any of the agents at our disposal that may reasonably be expected to help. Briefly to survey the help offered to the physician in his daily work by modern pharmacotherapy is the object of the present symposium. The time allotted will, of course, not permit of any detailed discussion of the use of single drugs. It is, I take it, the intention of those who planned the symposium that it should deal rather with the general principles that underlie the use of drugs in therapy, and with certain examples of the application of these principles in practice. Others are to speak of the use of drugs by surgeons and by specialists; this paper has to do with their use by the internist.

Man desiring to help his suffering fellow man must not lack—indeed, has never lacked—courage. Think, for example, of the boldness of the surgeon who annihilates the consciousness of his patient and then, without trepidation, cuts into the abdomen, or excises a goiter, or removes a brain tumor! The physician also must have bravery, one might almost say audacity, when he attempts, by the use of a drug, to intervene favorable in the disturbed physical, chemical and biologic processes of the human body in disease.

## COMPLEXITY OF CHEMICAL PROCESSES.

Man's body is the most marvelous chemical laboratory in the world, a laboratory made up of several thousand billions of separate work rooms, in each of which the amount and kinds of work done differ somewhat from those in each of the others. No two liver cells, probably, are precisely alike in their chemical activities. In a single mucous membrane, the chemistry of the constituent gland cells differs markedly from the chemistry of the constituent nerve cells, connective tissue cells and smooth muscle cells. Within the channels of communication that carry fluids and solids about the great laboratory from work room to work room, chemical changes are constantly going on in the transported materials. Even the walls, the beams and the furniture of the billions of work rooms are themselves constantly undergoing chemical change. We are awed enough by the complexity of the chemical processes that go on in health; but let us not forget that in the diseased body, which is the province of the pharmacotherapist, this complexity becomes manifold. Into this apparently infinite welter of chemical transformations (though, in reality, orderly and ultimately knowable) goes the drug that the physician administers in the hope of curing, regulating or ameliorating. Its administration surely signifies courage on the part of the physician who has such a conception of the body's chemistry. The task he attempts is truly Promethean. Is it not to try "to defy Power, which seems omnipotent?"

## THE DEVELOPMENT OF PHARMACOTHERAPY.

Man's needs have been so urgent, however, that medical men everywhere, and at all times, have not hesitated to defy powers when they seemed malevolent; and drug therapy has, despite its besetting difficulties, become one of the successful methods by which medicine "folds over the world its healing wings."

The clinical experience of the centuries slowly supplied an important body of facts regarding the nature of disease and man's power to control it, but the formation of true guiding principles for pharmacotherapy had to await the rise of modern science. More of value has been learned regarding rational treatment by the use of drugs in the last fifty years, perhaps, than in all the centuries that preceded; for, during the last fifty years, we have gained entirely new conceptions of the nature and causes of disease.

Through chemical, physiologic, psychologic, pathologic and clinical studies we have learned much regarding pathogenesis, that is to say regarding the chains of changes in the body that follow on injuries of various sorts. Synthetic chemistry has supplied us with a host of new substances for trial as remedies. The new sciences of pharmacology and toxicology have revealed to us the mode of action of drugs and poisons, and medical students are observing for themselves, in our pharmacologic laboratories, the physiologic effects that follow the introduction of foreign substances into the animal body, and they measure some of these effects with instruments of precision. Knowing only too well that, in the diseased body, drugs often act in an unexpected manner, in ways very different from those in which they act in the healthy body, clinicians have wisely seen that the pharmacology of the laboratory, though of great value for the general advance of scientific therapy, cannot take the place of accurate clinical observation. It can do much to guide therapeutic effort and to supply criteria for judging of its effects, but the final and crucial test of the value of any therapy is that of actual clinical experience. The clinic can help the laboratory, and the laboratory the clinic; but each has its independent domain that should be conscientiously worked and zealously safeguarded.

#### THE NEW EXPERIMENTAL SCIENCES.

Recently, laudable attempts partially to bridge the gap between the pharmacologic laboratory and the clinic, in the interests of pharmacotherapy, have been observable in the work of the new sciences of experimental pathology and experimental therapy, especially experimental substitution therapy, and experimental antiparasitic therapy (immunotherapy, serotherapy and chemotherapy).

Workers in these new sciences reproduce certain sharply circumscribed syndromes in experimental animals and then study various forms of treatment experimentally, analyzing the effects of the measures tried. With the advent of experimental pathology and experimental therapy, we can hope for the rapid development of a systematic science of therapy; and though the transfer of results of experiments in treatment of sick animals to treatment of the sick human being will always mean a leap from the known to the unknown, still this transit will from now on be made with ever lessened danger. New drugs and chemicals will in the future be thoroughly

and reliably tested, not only in pharmacologic laboratories on healthy animals, but, as far as possible, also in laboratories of experimental pathology and therapy, on animals in which special diseases have been induced, before we shall feel justified in making trial of them in the treatment of sick human beings.

#### CLASSES OF PHARMACOTHERAPY.

Now that physicians generally understand that, in all diseases or pathologic processes, they have to deal with modifications of normal (or physiologic) processes that depend on definite disease causes, modifications, moreover, that are beyond the self-regulating capacity of the organism to keep within those limits of functional activity that we observe in "health," the internist can classify his pharmacotherapeutic efforts according to the kind of effect he desires to produce. Thus, (1) he may try with a drug to remove the cause of the disease or to render it harmless (etiological pharmacotherapy); or (2) he may use a drug that will help directly to restore a pathologically disturbed function to normal (functional pharmacotherapy); or (3) he may administer substances that will aid the organism in its modes of reaction against the disease-cause (regulatory pharmacotherapy); or, finally, (4) he may employ drugs merely to relieve single troublesome symptoms (symptomatic pharmacotherapy). Internists who, after thorough and complete diagnostic studies, carefully consider these several indications (etiological, functional, regulatory and symptomatic) should achieve in their pharmacotherapy the highest possible success.

#### ETIOLOGIC PHARMACOTHERAPY.

Pharmacotherapy is seen at its best when, through the use of a drug, the cause of a disease is removed or rendered harmless (etiological pharmacotherapy) before the patient has sustained irreparable injuries. The organism can then right itself, so that its activities can resume their normal or physiologic course. As our knowledge of disease causes steadily undergoes increase, ever more maladies will be made accessible to etiologic therapy. Physicians of all times have considered the causal indication when they removed harmful substances from the stomach by emetics, such as mustard or ipecac, or from the intestine by purgatives, such as castor oil, calomel or magnesium sulphate. The greatest successes in causal therapy have,

however, been achieved by using drugs that kill living animal or vegetable parasites within the body, or that drive them from the body into the world outside. The use of oleoresin of male fern against tapeworm, of santonin against roundworms, and of oil of chenopodium against hookworms, are paradigms of antiparasitic pharmacotherapy. The parasites of malaria were killed by the quinin contained in cinchona long before we knew that the malarial fevers were parasitic in origin. Pathogenic amebas in the intestine can be killed off by means of emetin hydrochlorid. The fungi that cause blastomycosis and sporotrichosis die when subjected to the influence of the iodids. Noteworthy triumphs have recently been scored also by etiologic chemotherapy directed against certain parasites (trypanosomes, spirochetes and spirilla) that cause African sleeping sickness, syphilis, and relapsing fever. Through prolonged experimental work, parasiticides have been discovered that have a greater affinity for and toxic effect on trypanosomes and spirilla than on the body cells and organs; in other words, poisons that are more parasitotropic than organotropic can now be used to kill certain invading micro-organisms without too much injury to the invaded host. Arsphenamin and neo-arshpenamin help us greatly in the fight against syphilis, and are undoubtedly valuable additions to our pharmacopeia. With further studies of the parasitotropic qualities of various arsenical and antimonal compounds, we can reasonably hope for satisfactory means of control of a series of tropical diseases that up to recent times have defied the efforts of therapists.

In the antiparasitic treatment of diseases of bacterial origin, experimental chemotherapy has thus far been baffled. This does not mean, however, a permanent defeat. There is much to encourage investigators to continue their search for internal disinfectants that may be safely used. The body fluids and the body cells contain, and manufacture, substances that can kill bacteria. The chemical constitution of these bactericidal substances, we can feel sure, will ultimately be discovered; the substances will, later, be made synthetically and utilized in therapy. Moreover, toxic bacteriotropic substances that are foreign to the organism and innocuous for it will also doubtless be found and used. We already know that ethylhydrocuprein will kill pneumococci, though its deleterious effect on the optic nerve makes it unsafe as yet as a therapeutic agent. But who knows how soon some enterprising experimental chemotherapist may find a

related pneumococcicidal substance that is less harmful to the body, just as the discovery of the relatively innocuous spirillocidal arsphenamin succeeded that of the blindness-producing atoxyl?

#### FUNCTIONAL PHARMACOTHERAPY.

Though less ideal and important than etiologic therapy, much good can be accomplished by the internist who, making use of a so-called functional pharmacotherapy, tries to restore to normal some function that, through disease, has become disturbed or abolished.

This can easily be made clear by citing a few examples. Thus, a patient with valvular disease of the heart may get on well for years, thanks to the reserve force of his cardiac muscle. But, sooner or later, the function of the heart muscle begins to fail, and breathlessness, tachycardia, arrhythmia, passive congestion and edema appear. In digitalis, the pharmacotherapist possesses a remedy that, properly used, will often slow the heart rate and increase the contractility and tonicity of the muscular walls of the heart so that the circulatory insufficiency will disappear. Or, a patient in whom atrial (auricular) fibrillation exists may have the normal initiation and conduction of atrial stimuli restored by means of a few doses of quinidin. Or, again, a patient whose arteries are becoming sclerotic may have spasms of the coronary vessels and the severe pain of angina pectoris that can be relieved by dissolving a tablet of glyceryl trinitrate under the tongue, which, by dilating the pathologically contracted coronary arteries, removes directly a responsible functional disturbance. Similarly, we can relax the bronchospasm of a typical attack of bronchial asthma by the injection of a few minims of a solution of epinephrin (1:1,000), and we can spur the atonic wall of the intestine to contract in a postoperative case by means of a hypodermic injection of solution of hypophysis (pituitary extract). In all these instances we make use of a functional pharmacotherapy.

Another example may be chosen from the field of metabolism. Thus, in gout, uric acid is not adequately excreted by the kidneys, being retained in the blood or deposited in the tissues about the joints. The function of uric acid excretion by the kidneys can be temporarily increased by the administration of cinchophen or neocinchophen, substances that also exert an exceptionally efficient analgesic effect in acute attacks of gout.

What we know as "organ therapy" may also be regarded as one kind of functional pharmacotherapy. If dried thyroids, for example,

be given to a patient with myxedema (due to absence or defective function of the thyroid gland), the substance administered is capable of substituting for the function in abeyance and, in turn, of restoring to normal function those distant organs whose activities have undergone change through lack of the thyroid hormone.

#### REGULATORY PHARMACOTHERAPY.

Turning next to regulatory pharmacotherapy, that form of treatment in which we administer remedies with the object of "aiding the body to react against the disease-process or the disease-cause," a good example will be seen in the pharmacotherapy of acute nephritis. In a severe glomerulonephritis, water, salt and urea are no longer adequately excreted by the kidneys, being retained in the body. The body attempts to excrete these vicariously, through the digestive tract and the skin. The physician may aid this natural reaction of the organism by using (1) a drastic purgative, like compound powder of jalap, which produces copious watery evacuations, and (2) a powerful diaphoretic, like pilocarpin nitrate, which causes free sweating. Such purgation and diaphoresis support the activities of the normal regulatory mechanisms of the body and are therefore classed as examples of "regulatory" pharmacotherapy.

In the treatment of diphtheria with antitoxin, we also employ a regulatory therapy, for, on injection of the antitoxic serum, we support the normal reaction of the organism in its effort to produce chemical substances that neutralize the toxins of the diphtheria bacilli.

The treatment of a posthemorrhagic anemia by preparations of iron may serve as a third example of regulatory pharmacotherapy. The body reacts after severe hemorrhage by increased activity of the red bone marrow, regenerating red blood corpuscles rapidly. More iron may be required for this accelerated erythropoiesis than is available in the ordinary diet. The reactive regenerative process can be strongly favored by administering ferrous carbonate, say in the form of Blaud's pills.

#### SYMPTOMATIC PHARMACOTHERAPY.

Symptomatic pharmacotherapy, which neither intervenes in the disease process as such nor attacks its cause, is, however, a form of therapy that is by no means to be despised. Though it is directed

only toward single symptoms that injure or torment him, this therapy is highly important for the patient, and, when successful, is the ground for much gratitude on his part. There is scarcely a symptom that is complained of by patients that physicians have not attempted to influence by pharmacotherapeutic methods. And the relief that can be afforded in many instances thoroughly justifies the attention that is given to the *indicatio symptomatica*.

It is above all in the relief of pain and of various forms of mental and bodily discomfort that this is true. We would not willingly neglect the administration of morphin in renal colic; of acetylsalicylic acid in the arthralgias; of wine or beer to paralyze certain pathologic inhibitions and to bring needed relaxation; of heroin and codein in the racking cough of pneumonia; or of the various analgesics that are effective in migraine, in neuralgias, and in the lancinating pains of tabes. Though we may deplore the abuses of alcohol as a beverage, of purgatives in habitual constipation, of sedatives in the neuroses, and of hypnotics in insomnia, we all will admit that after causal, functional and regulatory indications have been as fully met as our science permits of, there will be occasions when the merely symptomatic indication dare not be ignored.

#### CONCLUSION.

It will be clear from what I have said that the internist looks on the use of drugs in therapy more hopefully now, perhaps, than ever before. Available drugs are of real value in curing, in ameliorating and in preventing disease, and new drugs that are useful are steadily being discovered.

Adequately to make use of the pharmacotherapeutic means at his disposal for meeting etiologic, functional, regulatory and symptomatic indications, the internist must, it is true, have mastery over a large body of facts. He must be well trained in normal and pathologic physiology and should have become acquainted with the known facts of etiology and pathogenesis. He should have learned in the pharmacologic laboratory the effects of the more important drugs on the normal animal body; and he should have had opportunity in the hospital wards, and in the laboratory of experimental pathology and therapy, to observe the changes that can be produced by drugs in disease. Very few have as yet had opportunity for the latter, but the medical schools should provide for it in the future.

Our teaching hospitals at present are, perhaps, more diagnostic institutes than institutes of therapy. It might, possibly, be wise to divide our medical clinics into two parts, patients entering one division for general diagnostic study and emergency measures, to be transferred afterward to the other division for full treatment, the effects of which could be carefully observed by the students.

The internist with such a training in the medical school as I have outlined will be prepared to institute a rational therapy wherever this is possible. He will know how to make a judicious use of empiric therapy when a rational foundation is lacking. As a matter of fact, pathology and therapy have of late years made such rapid strides that the physician can, in the majority of instances, give reasons for the therapeutic faith that is in him. For this we have to thank both the research activity of the scientific laboratories and the keen and critical observations of our better clinics.

The introduction of new therapeutic methods and new drugs can scarcely be expected from now on to be arrived at by accident, or through pure empiricism. Every new therapeutic agent should, as Magnus<sup>1</sup> has emphasized, be thoroughly tested in the laboratories as regards its activity and its dangers and, later, in the organized clinics, before it is introduced into general medical practice. But results in clinical experience must ever remain the final and crucial test of every form of therapy.

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#### THE DETERMINATION OF TANNIN.\* <sup>12</sup>

By JOHN ARTHUR WILSON and ERWIN J. KERN.

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A rather widespread controversy has arisen over a new method of tannin analysis described by the authors in two previous papers,<sup>2</sup> in which it was shown that the methods adopted as official both here

<sup>1</sup> Magnus, R.: *Allgemeine Pharmakotherapie*, in Krause and Garré: *Lehrbuch der Therapie der inneren Krankheiten*, Jena 1: 71-143, 1911.

\*Reprinted from the *Journ. of Ind. and Eng. Chem.*, September, 1921.

<sup>2</sup> Received July 26, 1921.

<sup>2</sup> To be presented before the Leather Chemistry Section at the Sixty-second Meeting of the American Chemical Society, New York City, September 6 to 10, 1921.

<sup>3</sup> *Journ. Ind. and Eng. Chem.*, 12 (1920), 465, 1149.

and abroad are greatly in error, exceeding 200 per cent. in some cases. Changing a method of analysis upon which millions of dollars of tanning materials are bought and sold annually is admittedly a serious matter. Were the new method to supplant the old in the sale of extracts, drastic price changes would have to be made and many extracts would no longer hold their present relative standings or reputation as to tanning value. Since the official methods have been clearly proved unreliable, it would seem that the new method must now be tested generally to determine whether or not it will meet all the conditions that ought to be required of a method so important. Until now its use has been restricted because the procedure as originally described was both cumbersome and time consuming, all of the first efforts having been directed exclusively to devising an accurate method. But the procedure has since been developed until it is now quite as simple as that of any method in general use. In this paper we describe the simplified procedure, and also refute the objections which have been raised against the new method.

#### DEFINITION OF TANNIN.

A thorough review of the literature shows that it has been generally agreed to class as tannin that portion of the water-soluble matter of certain vegetable materials which will precipitate gelatin from solution and which will form compounds with hide fiber which are resistant to washing. Much confusion would have been avoided in discussion by making it clear whether the criticism was directed against the definition or the method.

#### CHANGES IN PROCEDURE.

In the method as originally described, the tanned hide powder had to be washed by shaking with water for 30 min., squeezing through linen, and repeating with fresh water until free from soluble matter, which usually required about twelve washings. This is now accomplished with very little effort in a washing apparatus to be described later. The washed powder, after drying, was analyzed for water, ash, fat, and hide substance ( $N \times 5.62$ ), and the percentages of these subtracted from 100 gave the per cent. of tannin in the powder. It was suggested earlier that this figure might be obtained simply by noting the increase in weight of the dry powder after tanning and washing, provided the washing operation was

so conducted that no powder was lost, making the determination direct instead of by difference and increasing the accuracy for unskilled analysts. The new washing apparatus not only makes this possible, but reduces the amount of hide powder required for a determination to one-sixth.

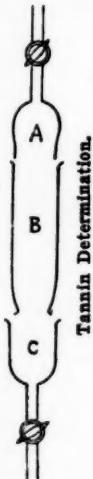
PRESENT PROCEDURE.

A solution of the tanning material is prepared of such strength that 2 g. of hide powder will detannize 100 cc. in 6 hrs. of shaking. With a little experimenting, safe limits are easily determined for all ordinary materials so that the need for repetition will be rare. For the extracts used in this work, suitable concentrations in grams per liter are 20 for hemlock, larch, oak, and sumac, 16 for gambier, and 7 for solid quebracho. The solution must be freed from insoluble matter, which may be done in the usual manner by adding kaolin, filtering through a thin paper, returning the filtrate to the paper for an hour to tan it, then discarding all liquor which has touched the paper, pouring fresh liquor on to the filter and collecting when the filtrate comes through clear. For materials which filter with difficulty, time can be saved by setting up several filters at one time. Standard hide powder,<sup>4</sup> or its equivalent, is extracted with chloroform to remove all extractable matter, and is then freed from solvent and stored ready for use. This treatment is chiefly to remove fatty matters, and it may be found convenient to treat a year's supply at once. Two grams of this powder, of known moisture content, are put into a 6-oz., wide-mouth bottle, 100 cc. of tan liquor are added, and the whole is put into a rotating box and shaken for 6 hrs. It is advisable to keep the liquor and wash water cool to guard against any tendency towards decomposition of the untanned portion of the hide powder. This matter requires attention only in hot weather.

The essential part of the washing apparatus is shown in Fig. 1 and consists of three glass parts fitting tightly into one another by means of ground joints. A small piece of fine filter cloth is stretched tightly over the bottom outlet of part B and is firmly secured by winding and tying strong thread around the groove. Parts B and C are then put together and the stopcock is opened. The tan liquor and hide powder, after the 6-hr. shaking, are washed into part B, the

<sup>4</sup> Prepared by the Standard Mfg. Co., Ridgway, Pa.

liquor being allowed to run through the open cock into a beaker and returned until reasonably clear.<sup>5</sup> The stopcock is then closed and B is half filled with water and then fitted to part A with stopcock closed.



The remaining part of the washing apparatus is a reservoir of water set high enough from the table to exert a pressure equal to a column of about 4 ft. of water upon the glass receptacle, which is connected to the reservoir by means of a rubber tube attached to A. The stopcock in A is opened wide, and the rate of flow of water is regulated to about 500 cc. per hr. by means of the stopcock in C, which is connected to the drain. Since the washing is usually complete in about 12 hrs., it is convenient to start it just before leaving the laboratory in the evening so that it will be complete at the start of the next day. However, washing should not be stopped until the wash water is colorless and does not darken upon the addition of a drop of ferric chloride.

The powder is then washed on to a Büchner funnel and freed from as much water as possible by suction. It is then allowed to dry in the air over night, after which it is completely dried in a vacuum oven for 2 hrs., desiccated and weighed. It is returned to the oven and reweighed as a check against insufficient drying. The increase in weight of the dry powder represents the amount of tannin present in 100 cc. of the original tan liquor.

We have found it very convenient to have rotating boxes capable of holding twelve bottles each and cylindrical stands equipped with twelve washing devices each. Given twelve filtered liquors Monday morning, the powders would be tanned and ready for washing before evening, ready for drying next morning, and the tannin values available before noon Wednesday. With one such outfit an analyst can easily complete twelve determinations every day and still have time for other work.

<sup>5</sup> This liquor must always be tested for tannin by adding one drop at a time, a freshly prepared solution of 10 g. gelatin and 100 g. sodium chloride per liter. A precipitate indicates that tannin is present, in which case the determination must be repeated, using a more dilute solution of the tanning material.

## COMPARATIVE ANALYSES.

The analyses of six typical extracts given in Table I show that there is practically no difference in results obtained by the original and revised procedures of the new method. Analyses by the official method of the American Leather Chemists Association, widely used in this country, are given for comparison.

TABLE I—COMPARATIVE ANALYSIS OF EXTRACTS BY A. L. C. A. METHOD AND THE ORIGINAL AND REVISED PROCEDURES OF THE NEW METHOD.

EXTRACT	A. L. C. A. METHOD			NEW METHOD		
	Water	Insoluble	Non-tannin (By Difference)	Tannin (By Difference)	Original Procedure (By Difference)	Revised Procedure (Direct)
Gambier .....	48.84	7.58	15.78	27.80	7.32	7.44
Hemlock .....	51.76	7.32	15.04	25.88	16.38	16.39
Larch .....	51.63	5.41	20.00	22.96	12.70	12.82
Oak .....	53.51	2.55	18.35	25.59	11.63	11.42
Quebracho .....	19.41	9.50	6.86	64.23	44.33	44.03
Sumac .....	49.44	2.86	22.56	25.14	13.10	13.04

## DISCUSSION.

A common objection to the new method has been that it appeared inconceivable that leather chemists everywhere should have been so misguided as to accept as official a method liable to a 200 per cent. error. The fallacy in the argument put forward lies in its assumption that leather chemists everywhere have found the official methods to be borne out quantitatively in practice. When data were called for to prove this assumption, apparently none were available. On the contrary, we have been able to secure data from both upper and sole leather yards showing that the amount of tannin appearing in the finished leather is very much less than entered the yards according to the A. L. C. A. method; and that the apparent loss of tannin corresponds closely to the difference in tannin content of the extracts as determined by the new and official methods.

After some experimenting with the new method, Schultz and Blackadder<sup>6</sup> raised a number of objections to it. Their first was that it was difficult to obtain concordant results, which they explained as being due in part to the fact that the tannin was determined by difference and was subject to the errors involved in determining the water, ash, fat, and hide substance in the tanned powder. This appears to us rather a matter of skill in manipulation, but in any event the cause has vanished with the revision of the procedure.

<sup>6</sup> *J. Am. Leather Chem. Assoc.*, 15 (1920), 654.

Their second objection was that the detannized liquor and wash waters gave a test for tannin when concentrated to small bulk. In an earlier paper<sup>7</sup> we showed that certain nontannins are converted into tannin when their solutions are evaporated and that this transformation can be followed by means of the new method, but not by the A. L. C. A. method.

Their third objection was that the degree of subdivision of standard hide powder is not uniform, that the finer portions become more heavily tanned but are more easily lost during the washing operation or in later handling, thus tending to give low results for tannin as a result of making the analyses on the portions of powder less heavily tanned. In the revised procedure no loss of powder during the washing is possible, and all of the powder is weighed after drying. It is worthy of note, however, that the results we obtained by the original and revised procedures are practically identical.

Schell<sup>8</sup> has raised an objection to the method that involves the definition of tannin. Following the work of Meunier,<sup>9</sup> he conceives the existence of two kinds of tannin which may be likened to quinone and hydroquinol. Meunier showed that quinone has tanning properties, while hydroquinol apparently has none. Given plenty of access to the air, however, solutions of hydroquinol become capable of tanning because of oxidation. According to Schell, the new method determines only the quinone-like tannin and fails to include hydroquinol-like bodies.

But hydroquinol admittedly has no tanning properties. It seems to us that the method is all the more accurate for not including as tannin, those bodies which are not tannin, although convertible by oxidation or otherwise into tannin. The existence of these substances in tanning materials has been recognized and discussed in our last paper, in which it was shown that the tannin content of a tan liquor is increased by boiling. There is good reason to believe that the new method can be developed to determine the amount of substances convertible into tannin as well as of actual tannin. This might be done simply by analyzing the liquor both before and after some special treatment, such as oxidation, that will convert into tannin all substances capable of such conversion. However, the data available to us indicate that only a fraction of these substances really appear as tannin in the finished leather.

<sup>7</sup> *Journ. Ind. and Eng. Chem.*, 12 (1920), 1149.

<sup>8</sup> *Le Cuir*, 9 (1920), 491.

<sup>9</sup> *Chimie & industrie*, 1 (1918), 71.

Schell is right in insisting that these nontannins have a value which should be recognized in judging the value of an extract, but the values should be recognized also of those substances which aid in the diffusion of the tannins into the hides and the sugars which form the necessary acids. Two extracts of apparently the same tannin content may have very different properties. The tannin content alone is no sure guide to the value of an extract; much importance is attached to the reputation of the extract manufacturer. It is not improbable that it will eventually be found preferable to sell extracts on a basis of total solid matter, leaving the extract men to compete with each other in establishing a reputation for producing extracts of high quality and constant composition.

In speaking of hydroquinol-like bodies, Schell implies the suggestion that what the official method really determines is the sum of these and the true tannins, but this is not so. Gallic acid belongs to the class of nontannins capable of conversion into tannin, but when added to a tan liquor only a variable fraction of it appears as tannin by the A. L. C. A. method, which makes the method quite unreliable and often very misleading. This is strikingly shown with gambier extract. The method calls for 12.5 g. of dry hide powder to detannize 200 cc. of tan liquor, which amount was assumed to be correct because the nontannin filtrate gave no test with the gelatin-salt reagent. Using this method on a gambier extract we found 26 per cent. tannin. But we then reduced the amount of hide powder to 1.5 g.; the nontannin filtrate gave a negative test with the gelatin-salt reagent, but the per cent. of tannin found was only 13. The extract is listed as containing 26 per cent. tannin simply because a group of men were more favorably disposed to make 12.5 g. of hide powder official than some other amount. This is treated more fully in our first paper.

The A. L. C. A. method is based upon a principle often employed in absorption experiments. It falsely assumes that the decrease in concentration of a tan liquor upon shaking with hide powder is a measure of the tannin content and that the solution absorbed by the substance of the hide is of the same composition as the remaining liquor. Thomas and Kelly<sup>10</sup> have shown to what ridiculous conclusions this can lead. In studying the effect of concentration of chrome liquor upon the adsorption of its constituents

<sup>10</sup> *Journ. Ind. and Eng. Chem.*, 13 (1921), 31.

by hide substance, they had occasion to use very strong liquors. Hide powder was treated with a chrome liquor containing 14.75 g. of chromic oxide per liter, but after 48 hrs. the concentration had risen to 15.40 g., although the hide powder had actually removed chromium from solution. This would correspond to a negative value for tannin by the A. L. C. A. method. What happened was that the hide powder absorbed a solution more dilute than the remaining chrome liquor and therefore concentrated the liquor more than enough to offset the chromium removed by combination with the hide substance. It is quite clear that one cannot determine the amount of matter removed from solution by noting the decrease in concentration of the liquor and calculating according to the instructions of the A. L. C. A. method.

#### SYNTHETIC TANNINS.

A representative of a firm manufacturing synthetic tanning materials of the Neradol type informed us that the use of the official method on their product meant nothing as it could be made to give any results desired. He was anxious to learn if the new method would indicate the per cent. of matter capable of forming a stable compound with hide substance. While we have done no work with syntans, as they are called, it is obvious that they differ from ordinary tan liquors in that they usually contain a large amount of free sulfuric acid. In using the new method on such materials there is the possibility that the acid might cause the hide substance to swell considerably during washing. This would slow down the washing action and tend to favor decomposition of hide substance, with a consequent loss in accuracy of the method. It seems possible that this might be avoided by using tap water saturated with salt for the first washings, until all sulfuric acid was removed, and then completing the washing with distilled water.

#### SUMMARY.

A modification of the authors' new method of tannin analysis is described which results in a great saving of time and labor, and tends towards increased accuracy.

Objections raised against the new method are refuted.

It is shown that the principle underlying the present official methods is unsound.

A suggestion for using the new method with syntans is made.

## NOTES ON ANCIENT MEDICINE.\*

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The science of medicine had its beginning in the mists of antiquity, and, in the absence of recorded facts concerning the very early times, it is not surprising that a mythology should have been developed with fanciful tales regarding such imaginary individuals as Apollo, Æsculapius, and Chiron. We know that the Egyptians transmitted to the Greeks much of the science they had used with advantage in the healing of the sick and wounded. Oracles were supposed frequently to indicate cures for diseased conditions, and temples were often places for the exchange of medical information; the priesthood of Greece caused tablets, certifying to cures, to be suspended in the temples where he that suffered might learn what had bettered the condition of another with a like affliction. Available literature tells us also that much was learned in early times by watching animals when laboring under disease: The goats of Crete are credited with having indicated the healing power of Dictamnus (wild marjoram); dogs, when indisposed, were noticed to seek triticum repens (couch grass—dog grass), and men were thus led to apply this drug to treatment of bladder inflammations; to the behavior of dogs mankind can also trace the first acquaintance with and use of purgatives; sheep known to have liver worms sought saline substances; cattle suffering from dropsical conditions were found to be benefited by drinking chalybeate waters; the hippopotamus is supposed to have taught the operation of phlebotomy (blood-letting), how, we are not informed; and from the sacred bird of Egypt, the ibis, the usefulness of enemata was learned. Among the Chaldeans and Babylonians a sick man was carried to a roadside where the passer-by might see him and tell what worked a benefit in the like condition in himself, his neighbor, his friend, or his aunt. It would appear that, in this respect, the ancients were pretty much like the people of today.

Much that is myth and fable concerning the science exists, but the first actual history goes back no further than the fourth century B. C. Hippocrates, a native of Cos, is thus the fountain head

\*From the *Supplement to the Naval Medical Bulletin*.

of all knowledge of medicine. The works of others who may have written before his time do not exist, and it is a further fact that all writings on medical subjects from the time of Hippocrates to the founding of the school at Alexandria by Serapion and Philinus, in the third century B. C., have also vanished; the school referred to is itself known only by references to it in other literature.

Then followed many writers on medicine and related sciences, some of whom were not physicians, so that the literature is clogged with "views" of persons who could not write with authority. To one going over some of the literature it seems that every philosopher felt himself capable of settling definitely mooted questions in medicine and, further, that every one who could write at all deemed himself a philosopher. It would be impossible in the scope of this paper to give a chronology noting the more important writers of ancient times on medical subjects; it should suffice to indicate in the proper places the times at which they lived.

Differences of opinion early led to the formation of several medical sects, the more important of which may briefly be noted here. The Dogmatici were apparently the parent-stock of our beloved allopaths of today; they approached the study of medicine in a truly scientific manner and later on more will be said concerning their division of the subject. Opposed to the Dogmatici were the Empirici and they were the first to cut into the practice of the "regulars." They founded the school at Alexandria, basing their teachings on what they termed The Tripod of Medicine, which consisted of observation (or autopsy), history, and analogy. Observation included what the practitioners noted during the course of an illness, history contemplated the written notes left by other writers in like conditions, and analogy or the substitution of one thing for another, was what they were thrown back upon when called to treat a case in which there was no precedent to follow, and the indications were obscure. Sagacity and sound judgment contributed greatly to the success of this sect, they had only to combat the vague, half-baked theories of the regulars, but their rejection of the study of anatomy, physiology and pathology made of them simply high-class experimentalists. Three of the followers (or leaders) of this sect, Sextus, Marcellus, and Plinius Valerianus, have left writings. As Marcellus lived in the fourth century A. D., the sect existed at least 600 years. Ignorant and indiscriminate experimenting is blamed as the cause for

their downfall, and the term empire eventually became a word of reproach. The Methodici, of whom Themison in the first century B. C. was the founder, attempted to steer a middle course between the two sects previously mentioned. Caelius Aurelianus was the principal writer of this sect and his book on acute and chronic illness is one of the most valuable of antiquity. The Episynthetici appear to have been a branch of the Methodici, which adopted for their own the best opinions of the other sects. It was founded about the year 100 A. D. by Agathinus of Sparta, and his pupil, Archigenes, is the father of the Eclectici. We are not informed as to the doctrines of the latter sect but they probably attempted to reconcile the tenets of the older sects.

Besides the school at Alexandria already mentioned, others were established at Cyrene in Africa, Crotona, Cnidos, Rhodes, and Cos. The latter is the most famous, as this town was the birthplace of Hippocrates, and from the school came many of the most eminent ancient physicians.

Before going into the subject of medicine it is well to note that the physicians and surgeons of early days had their troubles. There was, to speak mildly, a great deal of diffidence regarding the use of medicines at all, and often bitter antagonism. The physician had not only to develop a science from nothing, but it was also necessary to educate the public into the view that he was a real benefactor to society. Some of the antagonisms may be noted in the quaint and sometimes fanciful phraseology of sixteenth century English. I quote from Burton:

" 'Twas Plinies (first century A. D.) dilemma of old—every disease is either curable or incurable, a man recovers of it or is killed by it; both wayes physick is to be rejected; if it is deadly it cannot be cured; if it may be helped, it requires no physician; nature will expell it of it selfe."

"Plato (fourth century B. C.) made it a great signe of an intemperate and corrupt commonwealth, where lawyers and physicians did abound; and the Romans distasted them so much, that they were often banished out of their city, as Pliny and Celsus (contemporary of Pliny) relate, for six hundred years not admitted. It is no art at all, as some hold, no not worthy the name of a liberall science \* \* \* 'tis a corrupt trade \* \* \* no profession; the beginning, practice and progress of it, all is naught, full of imposture, incertainty, and doth generally more harm than good. The divel

himself was the inventor of it." Shaw, in his preface to "The Doctor's Dilemma," was not more hypercritical.

"Much emulation, imposture, malice there is amongst them (physicians); if they be honest and mean well, yet a knave apothecary, that administers the physick and makes the medicine, may do infinite harm, by his old obsolete doses, adulterine drugs, bad mixtures. \* \* \* But it is their ignorance that does more harm than their rashness; their art is wholly conjecturall (if it be an art), uncertain, imperfect, and got by killing of men: They are a kind of butchers, leeches, men-slayers; chirurgeons and apothecaries especially, that are indeed the physicians, hangmen and common executioners; though to say truth, physicians themselves are not far behind."

Thus while Burton quotes his authorities he is quick to make it plain that he does not always accept their points of view: "But I will urge these cavilling and contumelious arguments no further lest some physician might mistake me, and deny me physick when I am sick; for my part, I a well perswaded of physick; I can distinguish the abuse from the use in this and many other arts and sciences; wine and drunkenness are two distinct things."

Archagathus, who lived in the latter part of the third century B. C., was the first foreign surgeon to settle in Rome. At first he was well received, a shop was provided for him, and he was given the honorable title Vulnerarius (healer?). However, on account of the frequency with which he used knife and cautery, the Romans soon changed his title to Carnifex (executioner).

The science of medicine was, by the Dogmatici, divided into anatomy and physiology, aetiology, pathology, hygiene, symptomatology (including diagnosis), and therapeutics, which also included pharmacy, surgery, and the regimen to be followed in illness which was contemplated under the division of dietetics. In the following an effort will be made to show by notes and quotations some of the conditions that existed in early days, which will present to the reader a means for calculating the enormous strides which have been made in the development of the science.

Alcmæon, who lived about 540 B. C., was the first man who dissected animals; the dissection of the bodies of human beings did not come until a much later date. He is credited with having discovered the eustachian tube. He maintained that goats breathe

through the ear, and this belief is attributed to the supposition that the animal he was dissecting had had the ear drum destroyed.

Aristotle (fourth century B. C.) corrected the error of Alcmæon, but had himself certain delusions. He says that the hearts has three ventricles, that there are but eight ribs on each side, and makes no distinction between the arteries and veins; he also believed the brain was not provided with a blood supply.

An old description divides the body into two parts, the "contained" and "containing." The contained consisted of four humors, *viz.*, blood, bile, water and mucus or phlegm, to which was sometimes added serum (from urine), sweat and tears. There was further an imponderable subtle vapor called spirits, which was supposed to be a "common tye or medium betwixt the body and soul." This view was accepted by Hippocrates, later with certain modifications by Galen, and, to a certain extent, in much later times.

I have before me a work written in 1621 which does not show a great deal of advancement on Aristotle. The description of the anatomy of heart and lungs is interesting: "The heart though it be a sole member yet it may be divided into two creeks, left and right. The right is like the moon increasing, bigger than the other part, and receives blood from vena cava, distributing some to the lungs to nourish them, the rest to the left side to engender spirits. The left creek hath the form of a cone, and is the seat of life, which (as a torch doth oyl) draws blood unto it, begetting of it spirits and fire; and, as fire in a torch, so are spirits in the blood; and by that great artery called aorta, it sends vital spirits over the body; and takes ayre from the lungs, by that artery which is called venosa; so that both creeks have their vessels; the right two veins, the left two arteries, besides those two common ancractuous ears which serve them both, the one to hold blood, the other ayre for several uses. The lungs is a thin spungy part, like an oxe hoof (saith Fernelius), the instrument of voice; annexed to the heart to express his thoughts by voice. \* \* \* That it is the instrument of voice is manifest in that no creature can speak or utter any voice that wanteth these lights. It is besides the instrument of respiration, or breathing; and its office is to cool the heart by sending ayre unto it by the venosal artery which vein comes to the lungs by that aspera arteria (trachea?), which consists of many gristles, membranes, nerves, taking in ayre at the nose and mouth, and it likewise exhales the fumes of the heart."

Other notes would tend to indicate that there was confusion between the nerves and ligaments, as well as between arteries and veins. The author from whom the above was quoted appears to have been more intent on perpetuating the quaintness from the ancients than disclosing the best thought of his time.

The division of the "contained" portion of the body into four humors led Hippocrates to develop what is known as the humoral pathology, in which it is postulated that the stomach is the prime source of the humors, and sickness is the result of their appearance in other parts. Invasion by bile caused acute diseases; mucus or phlegm was the cause of catarrh and the rheumatic affections; dropsy depended upon water from the spleen. The quantity of bile determined the type of fever. Beginning with an extreme quantity of bile, and lessening the amount, the fever would be called continued, quotidian or tertian; a quartan fever was one in which the bile was mixed with viscous black bile (or atrabile). Both Galen and Hippocrates believed inflammation to be due to the introduction of blood into a part which had none before. If this introduction was complicated by mucus, bile, or atrabile the inflammation would not be pure, but would be known as cedematous, erysipelatous, or scirrhous, respectively.

Surgery came to the Greeks from the Egyptians and, as in medicine, Hippocrates stands forth as the first writer of note. He is credited with ten works on the subject, though some of them are regarded as spurious. When one considers the defective state of the knowledge of anatomy, the success of this surgeon is remarkable. He was skilled in treating fractures and dislocations, and was also familiar with the trephine. Asclepiades (first century B. C.) was first to propose the operation of bronchotomy, though he never performed the operation. Ammonius of Alexandria was first to propose and perform a lithotripsy—stone in the bladder having been a popular malady. Celsus has minutely described the operation from whose description the following may be of interest: "A hook is to be insinuated behind the stone so as to resist and prevent its recoiling into the bladder, even when struck; then an iron instrument is used, of moderate thickness, flattened toward the end, thin but blunt; which being placed against the stone, and struck on the farther end, cleaves it." After Hippocrates, this Celsus is the next important writer on surgical subjects. Qualifications laid down by him for

a surgeon is evidence that the patient was required to possess considerable morale: "He ought to be young, or at any rate not very old; his hand should be firm and steady and never shake; he should be able to use his left hand with as much dexterity as his right; his eyesight should be acute and clear; his mind intrepid, and so far subject to pity as to make him desirous of the recovery of his patient, but not so as to suffer himself to be moved by his cries; he should neither hurry the operation more than the case requires, nor cut less than is necessary, but do everything just as if the other's screams made no impression on him." Galen was the most voluminous writer on surgical as well as medical subjects. He practiced surgery at Pergamus, but when he moved to Rome in 165 A. D. he confined himself to medicine, following, as he said, the custom of the place. He believed that the physician should not invade the domain of surgery save in actual emergency.

Blood-letting was a frequent practice, but there were many contentions as to the conditions under which it should be done. The phases of the moon and aspects of the planets were taken into consideration; the morning was the best time of day for this operation. Cupping (dry and wet), horse leeches, the cautery, and issues (seton) were respected surgical procedures. In regard to blood-letting Sallust Salvian says: "If the blood abound, which is discerned by the fulness of the veins, his precedent diet, the parties laughter, etc., begin with the median or middle vein of the arm; if the blood be ruddy and clear, stop it; but if black in the spring-time, or a good season, or thick, let it run according to the parties strength; and some eight or twelve days after open the head vein, and the veins of the forehead, or provoke it out of the nostrils, or with cupping glasses." However, "Before you let blood deliberate of it and well consider all the circumstances belonging to it." Hippocrates is quoted as saying: "In melancholy and mad men, the various tumor or haemorrhoids appearing doth heal the same."

Something in the nature of a capital operation is indicated by the following: "Cauterries and hot irons are to be used in the suture of the crown, and the seared or ulcerated place suffered to run a good while. 'Tis not amiss to bore the skull with an instrument to let out fuliginous vapors." In another place the boring of the skull in two or three places is recommended as it "much availeth to the exhalation of the vapors."

Moderation in the use of medicines (or "physick") is emphasized by one writer: "A discreet and godly physician doth first endeavor te expell a disease by medicinall diet, then by pure medicine \* \* \* He that may be cured by diet, must not meddle with physick \* \* \* Whosoever takes much physick in his youth, shall soon bewail it in his old age, purgative physick especially which doth much debilitate nature."

It was at one time an accepted theory that each locality provided a medicinal substance for each diseased condition occurring therein, and those who adhered to this theory objected strenuously to importing medicines from distant lands. By the terms "simple" was understood a single plant, or a medicine prepared from such a plant, while compounds were what the name indicates. Burton states that many people favor the "exotick simples," such as, "sena, cassia out of Egypt, rubarbe from Bombay, aloes from Zocotra, turbith, agarick, mirabolanes, hermodactils from the East Indies, tobacco from the West, and some as far as China, hellebore from the Anticyræ, or that of Austria which bears the purple flower."

In condemning the use of imported and strange drugs we note that, "Many an old wife or country woman doth often more good with a few well-known and common garden herbs, than our bumbast physicians, with all their rare, prodigious, sumptuous, far-fetched, conjecturall medicines." This would suggest a tendency to use European medicines in preference to foreign ones; nevertheless, the domestication of plants from distant lands was commended and practiced in the public gardens at Padua, Leyden, Montpelier, Oxford, and Nuremberg. This culture was approved in order that "the young students may be the sooner informed in the knowledge of them which, as Fuschius holds, is most necessary to that exquisite manner of curing, and as great a shame for a physician not to observe them, as for a workman not to know his tools."

Galeottus appears to have recognized some 800 simples including those classed as alteratives which he defines as remedies that "by a secret force and speciall quality, expell future diseases, perfectly cure those which are, and many such incurable effects."

The water lily was esteemed for its anaphrodisiac qualities, cabbage was thought to resist drunkenness and, "that which is more to be admired, that such and such plants have a peculiar vertue to such

particular parts: as to the head—aniseed, foafoot, betony, calamint, eyebright, lavender, bays, sore, rue, sage, marjoram, piony, etc.; for the lungs—calamint, liquorice, enula campana, hysop, horehound, water germander, etc.; for the heart—orage, buglosse, saffron, bawm, basil, rosemary, violet, roses, etc.; for the stomach—wormwood, mints, betony, bawm, centaury, sorel, purslan; for the liver—darthspine, chamæpitys, germander, agrimony, fennell, endive, succory, liverwort, barbaryes; for the spleen—maidenhair, finger-ferne, dodder of thyme, hoppe, the rind of ashe, betony; for the joints—camomile, organ, rue, cowslips, centaury the less; and so on to particular diseases."

Some notes regarding the identity of drugs used by the ancients may not come amiss:

Turbith is also known as turpeth and is the dried root and stem of *Ipomea turpethum*. It is a purgative something like jalap but milder. It contains 10 per cent. of resin and a yellow coloring matter. It is said that the basic sulphate of mercury got its name "turpeth mineral" from its resemblance in color to the root.

Agarick is recognized as spunk touchwood or tinder, and is a fungus (*Polyporus officinalis*) growing on certain larches and pines, the best coming from Siberia. The active principle is agaric acid (agaricin) and, aside from the Solanaceous plants, is one of the best remedies we have for treatment of night sweats of phthisis.

Hermodactils was probably *Colchicum Illyricum*, or an allied species. It was also called Mercury's finger, and was a root shaped like a heart, flattened, and of a white color.

Betony or betonica was named by Pliny from the Vettone, a people of Spain, who discovered it. It belongs to the order Labiatæ and has been used as emetic and purgative.

Eyebright also called euphrasia, is a small annual plant of Europe. It was formerly used in the treatment of affections of the eye, hence its name. It is mildly astringent.

Under the head of calamint, *Calamintha officinalis*, *C. nepeta*, and *C. sylvatica*, were included. Strongly aromatic, they were much thought of by the ancients.

Enula campana, or elecampane, is the *Inula helenium*, the plant supposed to have sprung from the tears of Helen. The root is stimulant and aromatic.

Agrimony was so named from the Greek word signifying "a

speck in the eye," which condition was supposed to be cured by the plant. It belongs to the rose family and is a bitter astringent.

Dodder is a parasitical plant of the genus *Cuscuta* and lives by attaching itself to clover, flax, thyme, and other plants.

Borage is identified as *Borago officinalis*, the stems of which contain potassium nitrate and some other salts.

Bugloss appears to be *Anchusa officinalis*, the root, leaves, and flowers of which were at one time recognized in our United States Pharmacopeia. They are practically devoid of medicinal properties.

Bawm is identified as the leaves and tops of *Melissa officinalis*, and is without medicinal value, though a highly flavored essential oil is contained.

Black hellebore, which was formerly official, we recognize as a drastic, hydragogue cathartic. It was first discovered (so the story goes) by a shepherd named Melonpodius, who noted the behavior of his goats after they had eaten it, and applied the rhizome (some say the milk from female goats which had eaten of the plant) to the treatment of illness in Elige and Calene, daughters of King Proteus.

The ancients used so many drugs which today we find inert and practically useless, it must appear that the apothecaries of those days had more ability in compounding medicines, or else the vehicles commonly used were potent and had therapeutic value. Here is a testimonial to the value of wine of bugloss, which reads not unlike some of our recently popular patent medicines:

"An excellent cordiall, and therefore worthily reckoned up amongst those herbs which expell melancholy and exhilirate the heart \* \* \*. If taken steept in wine, if wife and children, father and mother, brother and sister, and all thy dearest friends should die before thy face, thou couldst not grieve or shed a tear for them."

Concerning a compound wine containing bugloss, borage, cinnamon, etc., it is stated, "It drives away leprosy, scabs, clears the blood, recreates the spirits, exhilirates the mind, purgeth the brant of those anxious, black, melancholy fumes, and cleanseth the whole body of that black humour by urine. To which I add (saith Villanovanus) that it will bring mad men such as are raging bedlamas, as are tied in chains, to the use of their reason again." The fourth ingredient appears to have added character to this compound.

Bawm was considered to "help concoction, to cleanse the braine, expell all careful thoughts and anxious imaginations."

Milady Nicotine comes in for extended consideration: "Tobacco, divine, rare, superexcellent tobacco, which goes so far beyond their panaceas, potable gold and philosopher's stones, a sovrain remedy to all diseases. A good vomit (emetic) I confess, a vertuous herb, if it be well qualified, opportunely taken, and medicinally used; but as it is commonly abused by most men which take it as tinkers do ale, 'tis a plague, a mischief, a violent purger of goods, lands, health—hellish, divelish, and damned tobacco, the ruine and overthrow of body and soul."

German frightfulness pales into insignificance before the story of Solon who, while laying siege to a certain city, "steeped hellebor in a spring of water which by pipes was conveyed into the town, and so poysoned or else made so feeble and weak by purging that they were not able to bear arms." Paracelsus also speaks of this drug and admired particularly the extract which he called, "The sole and last refuge to cure this malady, the gout, leprosy, etc."

If it were desired to marshal authorities on the use of wine in medicine, the ancient literature contains much material both for and against, though the objections were chiefly against excesses. Rhasis knew no better physic for a melancholy man and "he that can keep company and carous needs no other medicine." Avicienna, also an Arabian, goes further and advises the melancholy patient to drink and to "now and then be drunk; excellent good physick it is for this and many other diseases."

Another testimonial, this time to the efficacy of borage wine, will conclude this section: "My conscience bears me witness that I do not lye. I saw a grave matron helped by this means; she was cholerick and so furious sometimes, that she was almost mad and beside herself; she said and did she knew not what, scolded, beat her maids, and was now ready to be bound, 'till she drank of this borage wine and by this excellent remedy was cured which a poor forrainer, a silly beggar, taught her by chance, that came to crave an alms from door to door." It is to be deplored that before and after taking photographs are not available!

There was some difference of opinion as to the value of precious stones and minerals, and their application to the prevention and treatment of disease. In his tract against Paracelsus, Thomas Eras-

tus said, "That stones can work any wonders, let them believe that list; no man shall perswade me: for my part, I have found by experience that there is no vertue in them."

Potable gold, mercury, arsenic, and antimony were used to a certain extent, and Matthiolus holds "No man can be an excellent physician that hath not some skill in chymistical distillations, and that chronick diseases can hardly be cured without minerall medicines." Regarding antimony, a case is cited of a parish priest in Prague, Bohemia, who "was so far gone with melancholy that he doted and spake he knew not what; but after he had taken twelve grains of stibium (as I saw myself and can witness, for I was called to see this miraculous accident) he was purged of a deal of black choler \* \* \* yet it did him so much good that the next day he was perfectly cured."

Among the Romans who were high livers emetics were very popular and the taking of an emetic was frequently the prelude to a banquet.

Amulets and charms were much in vogue. Regarding the topaz it was said, "If it be either taken in a potion or carried about, it will increase wisdom, expell fear." Cardan brags that he hath cured many men with it which, "when they laid by the stone were as mad again as ever they were at first."

"In the belly (gizzard ?) of the swallow," says Burton, "there is a stone found, called chelidonium which, if it be lapped in a fair cloth, and tied to the right arm, will cure lunaticks, mad men, make them amiable and merry."

The carbuncle and coral were believed to "drive away childish fears, devils, overcome sorrows, and hung about the neck, repress troublesome dreams." Ruess ascribes the same qualities to the diamond.

Classified under precious stones are "the bone in the stag's heart," a "moncerot's horn," and the "Bezoar's stone." This latter is "found in the belly of a little beast in the East Indies" and "Rho-deus saith he saw two of these beasts alive in the castle of the Lord of Vitry at Coubert."

Among amulets, the following were guaranteed to give satisfaction: "A ring made of the hoofe of an asses right fore foot, carried about." The carrying of a spider in a nutshell wrapped in silk was thought "to keep off ague."

For epilepsy, "a piece of an old sailcloth taken from a shipwrecked vessel, to be tied to the right arm for seven weeks together."

For colic, "The heart of a lark to be fastened to the left thigh."

For a quartan ague, "A few hairs taken from a goat's chin."

"Pliny says that any plant gathered from the bank of a brook or river before sunrise, provided that no one sees the person who gathers it, is considered as a remedy for a tertian ague when tied to the left arm, the patient not knowing what it is."

"A person may be immediately cured of the headache by the application of any plant which has grown on the head of a statue, provided it be folded in the shred of a garment, and tied to the part affected with a red string."

Not quite so fanciful, yet not without interest is a remedy for the flatulence occurring in "hypochondriacal melancholy." It consisted in the use of a clyster pipe connected to a pair of bellows, concerning which, Burton simply comments that nature abhors a vacuum.

This paper concludes with a note on the subject of dietetics. Burton enumerates practically all foodstuffs of all times and then proceeds to quote authorities condemning all of them. With regard to beer, he quotes Crato as objecting to it as "windy because of the hop," and translates Henricus Abrincensis:

"Nothing comes in so thick;  
Nothing goes out so thin;  
It must needs follow, then,  
The drugs are left within"—

References: *Dictionary of Greek and Roman Antiquities*, Anthon. *Anatomy of Melancholy*, Burton.

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#### MODE OF ACTION OF SOME COMMON LAXATIVES.\*

Without doubt the common laxatives are the most widely used drugs in the entire pharmacopeia of the modern physician; hence the conclusion is irresistible that he should be adequately informed regarding their precise mode of action. If an added reason were necessary it could readily be found in the all but universal use

\*From the *Journ. of A. M. A.*, August, 1921.

of laxative drugs by the laity. Sometimes they are purchased by the public with a distinct appreciation of their purpose; not infrequently potent laxatives represent an essential ingredient of proprietary and "patent" medicines that are secret as to composition and misrepresented with respect to their pharmacology. Probably physicians would be more discriminating, or at least more rational in the prescription of the various laxative preparations, if information regarding the pharmacodynamics of the subject were more widely disseminated among the members of the profession.

Calomel is a popular representative of the group of non-saline laxatives. It has currently been represented to act by promoting intestinal secretion and retarding absorption, so that an accumulation of the abundant fluid and a consequent evacuation of semisolid contents ensues.<sup>1</sup> A recent investigation of the pharmacologic action of calomel, aided in particular by roentgen-ray observations of the progress of the alimentary reactions has not substantiated the view just cited. Working in the pharmacologic institute of the University at Utrecht van der Willigen<sup>2</sup> has concluded that absorption in the gastro-intestinal canal is not interfered with in the presence of calomel. The drug functions by promoting more vigorous movements of the small and large intestines whereby the contents are propelled so rapidly toward the rectum that absorption and the production of formed stools cannot take place. The fundamental feature in the action of calomel therefore, is its influence on alimentary peristalsis.

The widely used phenolphthalein, the laxative action of which was an accidental discovery of pharmacology, is another drug which promotes peristalsis so that fluid contents are driven into the proximal colon more rapidly than under normal circumstances. Van der Willigen has recently demonstrated that the drug does not retard absorption, nor does it produce secretion in undue quantities, as is currently taught. In connection with this laxative also, then, our present day assumptions must be revised.

How sulphur acts to promote purgation has been considerably debated. One investigator, for example, has believed that it gives

<sup>1</sup> Meyer, H. H., and Gottlieb, R.: *Experimentelle Pharmakologie*, Ed. 4, Vienna, 1920.

<sup>2</sup> Van der Willigen, A. M. M.: *Die Abführwirkung des Kalomels*, Arch. f. d. ges. Physiol. 186: 185, 1921.

rise to sulphurous acid which acts as an irritant in the bowel. In contrast with this is the finding of hydrogen sulphid in the lower small intestine and upper large bowel after ingestion of sulphur. The most recent investigator van der Willigen has adopted the hypothesis of the function of the sydrene sulphid as the potent factor. He thus pictures its action: Ordinarily the chyme which discharges from the small intestine into the colon is soon concentrated there by the rapid absorption of water; but when hydrogen sulphid is formed in considerable abundance from ingested sulphur it provokes a more rapid passage of the semi-fluid contents beyond the colon so that the usual concentration cannot take place. A corresponding change in the feces is observed along with the more rapid evacuation.

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#### THE POWER OF THE HEART.

A writer in the *Scientific American* has been doing some figuring as to the horse-power—he does not use this expression—of the human heart and he evolves some statistics which while of no practical importance, are interesting. Within each human breast, he says, this energetic organ is beating, on an average, about seventy-five times a minute, or 4500 times an hour. Accordingly, the heart beats, approximately 108,000 times daily, 39,000,000 times yearly, and, during a lifetime of three-score and ten years, two billion seven hundred million times. If we estimate the population of our world at 1,700,000,000 people, then all the human hearts on our terrestrial planet are beating at the rate of, approximately, 127,000,000,000 times a minute, or 66 quadrillion times a year. That is to say, these 1,700,000,000 human hearts are throbbing at a rate of about 2 billion times a second.

As we well know, our heart-engine contains four compartments, two auricles and two ventricles. The auricles are reservoirs which supply the pumping ventricles with blood. Therefore, the dynamic energy of the human heart resides in the right and the left ventricles. When these ventricles contract, the right ventricle sends its supply of impure blood to be purified by the oxygen in the lungs, and the left ventricle forces its supply of purified blood to circulate in the body. When the "heart beats," that is, when the right and left ventricles beat an average of about 10 cubic inches of blood

is expelled from the heart engine. Accordingly, in a minute, after seventy-five heart beats the energetic heart has pumped 750 cubic inches of blood. This means that the heart pumps 45,000 cubic inches of blood an hour, 1,000,000 cubic inches of blood a day, and 392,-000,000 cubic inches, or more than 225,000 cubic feet of blood each year. Were the heart a water pump instead of a blood pump, it would expel since a cubic foot of water weights about  $62\frac{1}{2}$  pounds, approximately, 7000 tons of water, during the course of one year.

And this amount of work is accomplished by only a part of a small muscular organ about as big as the average human fist! It has been estimated that the left ventricle alone exercises sufficient pressure per square inch to support a column of blood 9 feet in height, and that it performs daily an amount of work equal to 90 foot-tons. Were we able to collect in a cubical reservoir all the blood pumped by one heart-engine in one year, that reservoir would be about 61 feet in each of its three dimensions. Or, were a circular water-tower with a diameter of 50 feet, it would be somewhat more than 115 feet in height, and it would contain about 1,700,000 gallons.

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#### ANTIDOTING MERCURIC CHLORIDE POISONING.\*

The following mode of treatment in the antidoting of mercuric chloride poisoning has been sanctioned and recommended by the Naval medical authorities, and is alleged to be certain of its aim if its instructions are rigidly adhered to. [Adherence to these specifications seem to require the services of an entire hospital staff.—Ed.]

1. Administer the whites of three eggs beaten up in a quart of milk and then empty the stomach by siphonage.
2. Give 300 cc. of fresh calcium sulphide solution, containing 1 grain to 1 ounce of water by mouth.
3. Wash out the stomach with fresh calcium sulphide solution, 1 grain to 1 ounce of water.
4. Administer in powder or tablet 0.36 gram of sodium phosphite and 0.24 gram of sodium acetate. If this is not available, give the following:

\*From the *Naval Medical Bulletin*.

Sodium hypophosphite .....	1 gm.
Water .....	10 mils
Hydrogen peroxide .....	5 mils

Use ten times as much of the hypophosphite as poison taken. Give a copious lavage of stomach with the above antidote diluted twenty times. Give the above undiluted antidote every eight hours for two days.

5. Pour through the stomach tube after the above lavage a solution of 3 ounces of sodium sulphate and 6 ounces of water containing 5 grains of calcium sulphide. Let these solutions remain in the stomach.

6. Give intravenously after withdrawing 600 cc. of blood, 800 cc. of Fischer's solution or of bicarbonate-glucose solution.

Fischer's solution:

Sod. chloride .....	14 gm.
Sod. carbonate .....	20 gm.
Aq. dist. ....	qs. 1000 cc.

7. Wash out the stomach morning and night, giving by the mouth after each washing 5 grains calcium sulphide dissolved in 3 ounces of water. Continue this lavage until the stomach washings are free from mercury when tested by Elliott's method and until the urine is free from mercury.

8. Give high colon irrigations of warm water morning and night, using 8 gallons of water for each treatment.

9. Give a hot pack twice daily.

10. Give 8 ounces of milk every second hour.

11. Give every second hour 8 ounces of the following solution, by mouth, alternating with the milk:

Potassium bitartrate .....	dr. j
Sodium citrate .....	dr. j
Sucrose .....	dr. j
Lactose .....	dr. iv
Lemon juice .....	oz. j.
Boiled water .....	oz. xvj

12. Force the patient to drink large quantities of the alkaline waters, such as Celestin Vich or Kalak water

13. Give a low fat and low protein or high carbohydrate diet

for four weeks. Avoid salt in diet, as it increases absorption of the mercury.

14. Give by continuous protoclysis a solution containing 1 dram of potassium acetate, 4 drams of glucose, and 3 drams of sodium carbonate to the pint.

15. Keep the urine alkaline to methyl red.

16. Continue rest treatment until recovery, usually a period of three weeks.

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#### HAINES MODIFIED TEST FOR GLUCOSE.\*

As far back as 1874, W. S. Haines<sup>1</sup> introduced a test for sugar in the urine which was regarded as more delicate than the methods in common use. Recently the same investigator, together with G. P. Pond and R. W. Webster,<sup>2</sup> published an improved test capable of detecting with certainty amounts about 0.03 per cent. of sugar, which is about the upper limit of the so-called "normal" sugar of the urine. That is, pathological sugar will be indicated, but physiological sugar will go undetected.

The composition of the improved Haines solution is:

Copper sulphate .....	5 gm.
Glycerin .....	250 cc.
Potassium hydroxide .....	20 gm.
Distilled water to .....	1000 cc.

The copper sulphate is dissolved in a mixture of the glycerin and an equal amount of water, with the aid of gentle heat. The potassium hydroxide should be dissolved in about 200 cc. of water and added to the copper solution with constant stirring, the whole being made up to volume with distilled water. This solution keeps indefinitely, although with many of the specimens of glycerin now obtainable on the market a reduction may be observed. If, however, the solution be allowed to stand in a warm place for forty-eight hours, the clear supernatant fluid may be decanted or filtered from the precipitated cuprous oxide, without impairing its delicacy.

\*From *The Prescriber*, 1921, p. 291.

<sup>1</sup>Med. Examiner, Dec. 1, 1874, p. 569.

<sup>2</sup>J. Amer. Med. Assoc., Jan. 31, 1920, p. 301.

The glycerin increases the specific gravity of the solution, and thus admits of the test being applied as a contact reaction in the following manner: Heat 5 cc. of the solution to boiling in a test tube; then remove from the flame and hold at an angle of 40° and add carefully from a medicine dropper 10 to 20 drops of urine freed from phosphates as shown below. Place the tube in a rack and observe the reaction. If sugar is present in quantity exceeding 0.1 per cent., a brick-red or yellow ring appears at once at the junction of the two liquids. Less than 0.1 and over 0.03 per cent. will show a ring in from a few seconds to a minute; the smaller the quantity of sugar the longer will the ring take to form and the more yellow will be its color.

Before applying the test the urine should be freed from phosphates by the addition of a few drops of solution of KOH (5 or 10 per cent.), allowing the precipitated phosphates to settle. This makes the test more delicate and is necessary to obtain reliable results; when the proportion of sugar is high the reaction will appear without previous removal of phosphates.

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REPORT OF THE SEMI-ANNUAL MEETING OF THE  
PHILADELPHIA COLLEGE OF PHARMACY AND SCI-  
ENCE, HELD AT THE COLLEGE ON SEPTEMBER 26,  
1921.

The meeting was called to order by the First Vice President, Mr. Rohrman, at about three o'clock. The minutes of the previous meeting were read by the Secretary. Mr. Rumsey suggested that the resolutions presented by Mr. Wetherill at the last meeting be expunged from the minutes. Chairman Rohrman ruled that the resolutions referred to were a proper part of the minutes of the previous meeting in as much as they were adopted by a nearly unanimous vote of the members present at that meeting and that they should therefore be retained in the record. This ruling of the chairman stood and the minutes were approved as read.

The minutes of the Board of Trustees were then read by Mr. Beetem, Secretary to the Board. Mr. Osterlund moved that the minutes of the meetings of the Board of Trustees held on June 7

and August 24 as read at this meeting be and hereby are approved and the action taken at the said meetings be confirmed and adopted by the corporation. Dr. Mattison suggested that it was unnecessary to approve the minutes of the Board of Trustees if they are correct and accurate. Mr. Osterlund replied that his motion was in conformity with the college by-laws which require action by the college upon the minutes of its Board of Trustees. A vote was then taken on Mr. Osterlund's motion and carried by a large majority.

There was no unfinished business.

The following reports of committees were then presented:

Committee on By-Laws, by J. W. England, chairman, reported progress.

Committee on Resolutions to Retiring Officers, by J. W. England, chairman, reported progress.

Committee on Nominations, Mr. John K. Thum, chairman—in the absence of the chairman this report was read by the Secretary.

"To the Recording Secretary,

Philadelphia College Pharmacy and Science.

Dear Sir :

The Committee on Nominations submits the following names for the list of offices to be filled at the stated meeting of the Philadelphia College of Pharmacy and Science on the fourth Monday in September, 1921 :

For President ..... William C. Braisted

For Board of Trustees—Five to be elected.

\*Richard M. Shoemaker, Ph. G. term expired.

Henry K. Mulford, Ph. G. term expired

Jacob M. Baer, Ph. G. term expired

George D. Rosengarten, Ph. D.

C. Mahlon Kline, Ph. B.

Walter V. Smith, Ph. G.

George B. Evans, Ph. G., to fill the unexpired term of Walter A. Rumsey, resigned.

Very truly yours,  
JOHN K. THUM, Chairman."

The Secretary then read letters of withdrawal as candidates for the Board of Trustees from Mr. J. M. Baer and Mr. H. K. Mulford.

\*In a note attached to the report the nominating committee submitted the name of Charles H. La Wall to fill the vacancy in the list of nominees occasioned by the death of Mr. R. M. Shoemaker which occurred subsequent to the first meeting of the committee.

Doctor Mattison moved that the name of Mr. Howard B. French be added to the report of the nominating committee as a nominee for the office of President of the College.

The Chair declared this out of order as no motion had been made that nominations from the floor be opened. The Chair stated it as his opinion that this privilege should be granted to any one desired to nominate from the floor and said that he would entertain a motion to that effect. Doctor Mattison then moved that nominations from the floor be opened. The motion was seconded by Professor La Wall and was carried unanimously.

Doctor Mattison placed in nomination the name of Mr. Howard B. French for President. The nomination was seconded by Mr. George M. Beringer.

Mr. Peacock moved that nominations be closed. This motion was duly seconded and carried.

Mr. George M. Beringer directed attention to the vacancy left by the resignation of the Treasurer of the College and moved that nominations be opened for Treasurer. Professor Stroup moved that nominations be reopened. The motion was seconded and carried. Mr. Beringer then placed in nomination the name of Mr. Milton Campbell for Treasurer of the College which was properly seconded.

Mr. Beringer stated it as his opinion that Mr. Osterlund was no longer a member of the Board of Trustees by virtue of his resignation from the office of President of the College, and moved that nominations for the Board of Trustees be reopened. The Chair stated that Mr. Osterlund was not functioning as an ex-officio member of the Board but that he had been regularly elected as a trustee of the College and had not relinquished that office. Mr. England stated that he had consulted the College Solicitor, Mr. McKaig, as to the legality of Mr. Osterlund's position on the Board and that the solicitor had confirmed the impression that Mr. Osterlund is a qualified member of the Board of Trustees by reason of his election thereto.

Mr. England moved that the body go into election of officers and members of the Board of Trustees. The motion carried.

Mr. Beringer stated that the custom of the College in recording the members present was not being followed and the Chair directed his attention to the fact that the members were being registered at that moment.

The Chairman appointed the following election officers: Messrs. J. J. Bender and J. N. G. Long as Tellers and Otto Kraus as Judge. Mr. England moved that as each member of the College voted his name on the membership list be checked off. This motion carried. Ballots were then distributed and the Chair directed attention to the fact that the name of Mr. Milton Campbell did not appear upon the ballots which had been prepared and should therefore be inserted by those voting.

At this juncture Doctor Mattison stated that he had had legal advice on the matter of Mr. Osterlund's status as a member of the Board of Trustees and as long as there was a question he desired to nominate Mr. Osterlund for membership to the Board. Chairman Rohrman declared the motion out of order. Mr. Beringer made an appeal from the decision of the Chair on the question. Chairman Rohrman stated that he had ruled that Mr. Osterlund is a bona fide member of the Board of Trustees. On motion, the ruling of the Chair was sustained by a large vote, a scattered few supporting the appeal from the decision.

In order to facilitate the election the Chairman was asked to appoint an additional member and Mr. Peacock was appointed to assist the other election officers.

Upon completion of the count of the ballots cast, the election officers presented the following report:

"We, the undersigned Judge and Tellers, appointed to conduct the election, at the Semi-Annual meeting of the members of the Philadelphia College of Pharmacy and Science, held on September twenty-sixth, nineteen hundred and twenty-one, report that votes were cast for the following persons:

For President:

Howard B. French,	15	votes
William C. Braisted,	146	"

For Treasurer:

Milton Campbell,	161	"
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For Trustees:

George B. Evans,	161	"
George D. Rosengarten,	161	"
C. Mahlon Kline,	161	"
Walter V. Smith,	161	"
Charles H. La Wall,	161	"

JOHN N. G. LONG, Teller,

JOHN J. BENDER, Teller,

OTTO KRAUS, Judge of Election.

OTTO KRAUS, Notary Public."

Nov., 1921.

The election officers were properly sworn and the notarial seal attached to the report by Notary Kraus.

Following presentation of this report Chairman Rohrman declared the following gentlemen to be properly elected to fill the respective offices in the College:

President: William C. Braisted. Term expires March, 1922.

Treasurer: Milton Campbell. Term expires March, 1922.

For three-year terms as trustees:

George D. Rosengarten,  
C. Mahlon Kline,  
Walter V. Smith,  
Charles H. La Wall.

To fill the unexpired term of Walter A. Rumsey, resigned:  
George B. Evans. Term expires September, 1923.

The Chair appointed a committee consisting of Messrs. Osterlund, Blackwood and La Wall to proceed to the Bellevue-Stratford and escort President Braisted to the College.

Professor Cook, on behalf of the donors, presented to the College the following gifts which had been received during the summer from members and friends of the College. These consisted of:

From Mr. William A. Whittem, of Chestnut Hill, Pa.: A stone Mortar given to Mr. Whittem, many years ago, by Mr. Wetherill, of the paint firm.

A wooden Mortar and Pestle, which Mr. Whittem thinks was used during the Civil War in the hospital at Bungtown, now Wyndmoor, and which was given to him by the late Dr. William Moss, who, with Doctor Gross, was stationed at that hospital.

From Dr. J. B. S. Egee, South Hampton, Pennsylvania: An iron Mortar and Pestle.

From Mr. George B. Evans, Philadelphia, Pa.: A wooden Mortar and Pestle which Mr. Evans picked up in his travels.

It was moved that the thanks of the College be conveyed to the foregoing list of donors by the Secretary when acknowledging the receipt of the gifts.

Upon motion of Professor Stroup, duly seconded and carried, the Board of Trustees was instructed to take up with the proper authorities the paving of the street to lessen the noise.

Upon motion by Doctor Mattison, seconded by Doctor Robinson and carried, the Board of Trustees was instructed to consider the matter of placing double windows on the front of the building to keep out the street noises. Chairman Rohrman stated that the matter of paving the street had been taken up with the city authorities and that the Mayor had promised his support in the work.

At this juncture President Braisted, accompanied by the Committee of escort entered and Chairman Rohrman, in greeting him, said: "It is my pleasure to inform you that you have been elected to the Presidency of the College. You have made a reputation in your other fields of endeavor, and the present financial and physical condition of the College fully convinces us that your reputation is justified. You will have behind you a harmonious Board of Trustees and a no less harmonious faculty, who are not only willing, but eager to render their services to you and all that is within their power.

Before turning this meeting over to you I wish personally to wish you God-speed in your hopes for this College.

Members of the Philadelphia College of Pharmacy and Science, our President."

In assuming the Chair, Doctor Braisted said:—

"Members of the College, from the remarks of the Chairman, Mr. Rohrman, I take it that after your careful deliberations of this afternoon and with due consideration from all points of view you have elected me to be your president I want to express to you my full appreciation of the high honor conferred on me by this action and to thank the Chairman for his splendid words of assurance of support from the College as a whole, from the Board of Trustees and the officers and faculty of the institution—I shall need your help, advice and assistance in the months to come in the great work before us and it is my view that no policy or action affecting the College or the profession of Pharmacy shall be taken by me without the hearty approval and direction of the various bodies concerned.

"I should love to discuss here today, at length the many issues before us but feel that the hour is so late that I may not trespass further on your time and patience.

"The first step in the work, the rehabilitation of the building and the expansion of the Educational programme has been accomplished during the past summer. How successfully this has been done and how it has been accomplished is known to you and the evidence of

the work done meets your eyes on every hand. No further reference to this is needed by me. Much time and thought has been and will be given to the remainder of the work including the future of the College, the raising of funds, the promotion of the interests of Pharmacy as a major science and profession, the closer relation of Pharmacy and Medicine and you will be kept informed as the work progresses and at the proper times of contemplated and accomplished work. When the extent of the work is reviewed involving as it does so many difficult and delicate problems I confess to some degree of apprehension as to my ability to carry out the part of the programme you have given me—but if we can have happy, kindly, interested and hearty co-operation by our entire body, we may achieve results far beyond our most sanguine hopes and the future of this splendid institution may ever transcend, in usefulness and splendid humanitarian work, and the record of the past of which we are all so proud. I thank you gentlemen for your confidence in me and shall do the best I can to deserve your approbation and to carry to a successful issue your desires and hopes in the profession that you honor."

Following prolonged applause the meeting adjourned.

AMBROSE HUNSMERGER, PH. G.,  
*Recording Secretary.*

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## SCIENTIFIC AND TECHNICAL ABSTRACTS

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CARBON MONOXIDE POISONING IN CLOSED GARAGES.—In this article attention is called to the fatalities occurring as the result of inhaling carbon monoxide from the exhaust gas of automobile engines running in small, closed garages. As this is not an infrequent item of news in the winter months, the public, particularly automobile owners and garage workers are warned of the danger in running a gasoline engine in a small, unventilated space.

In connection with experiments having to do with the problem of ventilation involved in the proposed vehicular tunnel under the Hudson River, several interesting facts have been demonstrated.<sup>1</sup>

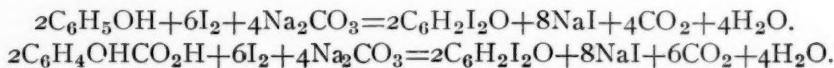
<sup>1</sup> Physiological Effects of Automobile Exhaust Gas and Standards of Ventilation for Brief Exposures. Yandell Henderson, Howard W. Haggard, Merwyn C. Teague, Alexander L. Prince and Ruth M. Wunderlich. *Jour. Ind. Hyg.*, July, 1921, pages 79-92, and August, 1921, pages 137-146.

I—Carbon monoxide is the only considerable toxic substance in the exhaust gas from gasoline. From benzol and illuminating gas, accessory poisonous substances result in the exhaust.

II—A concentration of 15 parts of carbon monoxide per 10,000 parts of air is dangerous to life.

III—If a car while "warming up" should give off 1 cubic foot of carbon monoxide per minute in a closed room 10 by 10 by 20 feet, the atmosphere would reach the dangerous concentration of 15 parts per 10,000 in three minutes, R. P. F.—(Abstracted from *Pub. Health Reports*, United States Public Health Service, Vol. 36, No. 36, Sept. 9, 1921.)

**ESTIMATION OF SALICYLATES AND PHENOL.**—In a method proposed for the estimation of these compounds advantage is taken of the characteristic behavior of the constituents phenol and salicylic acid towards iodine; the final product of the reaction in the presence of alkali or alkaline carbonate is a purplish-red amorphous compound  $C_6H_2I_2O$ , termed diiodophenylene oxide or tetraiodophenylene quinone. The reaction is represented by the equations:



Each molecule of phenol, salicylic, or acetylsalicylic acid yields one molecule of the iodine compound, whilst one molecule of salol yields two molecules of the same compound. In the case of salol, about 0.1 gm. of the sample is weighed on to a small dry filter and washed with successive quantities of chloroform until all soluble substances have been dissolved; the chloroform solution is evaporated at the ordinary temperature in a conical flask, the dry residue obtained is treated with 10 cc. of a 1 per cent. sodium hydroxide solution, and the mixture heated under a reflux apparatus so that boiling begins in about two minutes. Successive quantities of 10, 30, and 50 cc. of water are then added, the heating being so regulated that the mixture begins to boil in about 3, 5, and 10 minute intervals respectively. Just before the last addition of water, 1 gm. of dry sodium carbonate is introduced into the top of the condenser and washed down with the water. To the clear boiling solution is now added 60 cc. (or an excess) of N/5 iodine solution, the mixture again boiled, the condenser then rinsed with a small quantity

of water, and the flask disconnected. A further 1 gm. of sodium carbonate is added, and the mixture boiled gently for 20 minutes; care must be taken during this period, as the evolution of carbon dioxide causes much frothing. The precipitate is then collected on a weighed filter, washed with not less than 200 cc. of hot water, dried at 100° C. and weighed. The weight found is multiplied by 0.3113 to obtain the amount of salol present. Acetanilide, phenacetin, and caffeine do not interfere with the estimation, but when phenacetin is known to be present, the quantity of iodine should be increased by 5 cc. for each 0.1 gm. of phenacetin. With a mixture of salol and acetanilide, the filtrate from the precipitate is practically colorless; but when phenacetin is present the filtrate is colored light yellow, so that it is not easy to recognize whether or not an excess of iodine is present.—Emery (*J. Ind. Eng. Chem.*, 1921, pp. 538-539, through *Analyst*, 1921, p. 376).

ESTIMATION OF LECITHIN.—In Hager's method of estimation the lecithin is decomposed by boiling with nitric and sulphuric acids, and the phosphoric acid precipitated with ammonium molybdate. The precipitate is washed, suspended in water, and dissolved in semi-normal alkali hydroxide solution, an excess of 5 to 6 cc. being added, and the solution boiled until all ammonia is expelled, and then titrated with semi-normal hydrochloric acid. Each cubic centimetre of decinormal alkali corresponds (according to Hager) with 1.268 mgm. of  $P_2O_5$ . The author finds this method tedious and quite unreliable. The phosphoric acid may be estimated directly in the residue obtained after removal of organic matter by a mixture of nitric sulphuric acids. The acid is first neutralized with alkali, and ammonium chloride and ammonia are added until a precipitate forms, which is then dissolved in dilute hydrochloric acid. Magnesia mixture is added, and the solution is treated with ammonia at boiling temperature. It is not possible, however, to determine the amount of lecithin in a sample from its  $P_2O_5$  content, as the formula  $C_{42}H_{84}NPO_9$  is doubtful.—(J. L. B. VAN DER MARCK, *Pharm. Weekblad.*, 1921, 989-992, through *Chem. and Drugg.*)

FAT-SOLUBLE VITAMIN AND YELLOW PIGMENTATION IN ANIMAL FATS.—There is a very high concentration of the fat-soluble vitamin in cod liver oil, but only small amounts of yellow pigments.

Butter fat shows a seasonal variation in the fat-soluble vitamin content when obtained from stall-fed cows during the winter and pastured in the summer. The fat-soluble vitamin content of butter fat does not run closely parallel to the yellow pigment; yet, in general, due to determination by their content in the feed, butters highly pigmented are rich in the vitamin; butters low in pigment should be looked upon with suspicion. In beef fats the relations are somewhat similar; those most pigmented are also generally richest in their fat-soluble vitamin content. The fat-soluble vitamin withstands severe methods of saponification. This indicates that it is not a fat, and probably not an ester.—(H. STEENBOCK, M. SELL and M. V. BUELL, [Journ. Biolog. Chem., Baltimore, June, 1921, p. 89; through Journ. Amer. Med. Assoc., July 9, 1921, p. 152.] )

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**INSECT POWDER DERMATITIS.**—An occupational dermatitis has been found to occur among the workers engaged in the manufacture of pyrethrum insect powder. Chemical analyses of pyrethrum have established various constituents having irritant properties. The lesions noted are, essentially, various forms of dermatitis venenata. They are of mild severity and quickly disappear under ordinary treatment. Re-exposure frequently leads to the reoccurrence of the disease. This dermatitis may be prevented by the introduction of trade processes that eliminate the necessity of exposure of workers to pyrethrum dust and powder.—(Through Journ. Amer. Med. Assoc.)

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**EFFECT OF COLD AND FREEZING ON CERTAIN PREPARATIONS.**—E'we has studied the effect of freezing upon magnesium magma and finds that after freezing and thawing the normal water content of the magnesium hydroxide gel is changed, with the result that molecules of magnesium hydroxide unite to form a fine crystallized powder. This formation is practically irreversible and cannot be brought back to the colloidal state. Other pharmaceutical preparations are likewise affected by freezing; Magma of bismuth subcarbonate, elixirs containing terpinol hydrate, Fowler's solution, compound solution of sodium phosphate, compound solution of hypophosphites, and solution of hydriodic acid, solution of ferrous iodide, and solution of hydrogen peroxide.—(Amer. Druggist.)

A NEW ANTIFEBRILE FROM INDIA.—Investigations are being made at present into the medicinal properties of a forest tree indigenous to parts of Bihar and Bengal that recall the circumstances under which quinine became known to the world as a remedy for malarial fever. The late civil surgeon of Ranchi, Lieut. Col. J. C. S. Vaughan, having noticed the occurrence of a large number of cases of malignant malaria and blackwater fever in that district, made inquiries among the aboriginal tribes to find whether they used any local plants as a cure for these diseases. It appears that there is a tree whose leaves, bark, and root are all used, and experiments that have been made with the leaves raise the hope that they may prove to be a valuable addition to our stock of drugs for use in the Tropics.

The tree is known by various vernacular names, but its botanical name is *Vitex peduncularis*. It is found not only in Chota Nagpur but also in eastern Bengal and the Khasia Terai. The simplest way to use it is to make an infusion of the leaves—1 ounce of leaves to 40 ounces of infusion. The effect has been found to vary, but this is true of quinine as well, and of most other drugs. In most cases larger doses or stronger infusions proved effective where the ordinary treatment had failed, and microscopic examination proved that the malarial parasites disappeared from the blood under the influence of the treatment. As these results have been obtained by using the drug in its crudest state, it is hoped that in concentrated form it may prove even more satisfactory. It has advantages over quinine in having no bitter taste or toxic properties, of being a stimulant rather than a depressant, and of being suitable for children and for people in delicate health. It is said to have been useful in influenza, and in cases of blackwater fever it has given very good results.—(Through *Commerce Reports*, June, 1921.)

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SWEETENING AGENTS; DEFINITIONS AND UNITS IN CHEMISTRY OF—. T. Paul. *Chem-Zeit.*, 1921, 45, 705-706.—The "degree of sweetness," SG (*Süssungsgrad*), of a substance is defined as the number of g. of pure sucrose which, in a given volume of water, has the same sweetening effect as 1 g. of the substance. The degree of sweetness of dextrose was found to be 0.52, that of lactose 1.03, lactose 0.28, mannitol 0.42, and that of a starch syrup containing 78 per cent. of solids 0.26; these values appear to be inde-

pendent of the concentration, at least for sucrose concentrations between 20 and 100 g. per l. For saccharin and dulcin, SG diminishes with increasing concentration, the values corresponding to sucrose concentrations of 20, 60, and 100 g. per l. being 667, 316, and 187 in the case of saccharin, and 364, 90, and 70 respectively in the case of dulcin. The degree of sweetness of a mixture of saccharin and dulcin is greater than that calculated from the values for the ingredients; e. g., 280 mg. of saccharin and 129 mg. of dulcin, in a litre of water, have the same sweetness as 535 mg. of saccharin alone in the same volume. The "sweetening unit," SE (*Süssungseinheit*), of a substance is defined as the number of g. required to produce the same effect as 1 kg. of sucrose, in a given volume of water.—(J. H. L.; through *The Analyst*.)

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GLYCEROPHOSPHATES; DETERMINATION OF SMALL QUANTITIES OF PHOSPHATES IN —. J. L. Lizius. Brit. Pharm. Conf., June, 1921. *Pharm. J.*, 1921, 106, 478-479.—One gm. of the glycerophosphates is dissolved in 50 cc. of water and the solution is added from a burette to a mixture of 10 cc. of 25 per cent. nitric acid and 10 cc. of 10 per cent. ammonium molybdate solution until the coloration obtained is equal to that produced by a known amount (e. g., 0.0002), of phosphoric acid in the same amounts of reagents. If 10 cc. of the glycerophosphate solution is required, the sample will contain 0.1 per cent. of phosphoric acid in inorganic combination. To apply the method to ferric glycerophosphate, the sample is dissolved in dilute nitric acid, heated, treated with sodium hydroxide, the ferric hydroxide separated by filtration, the filtrate diluted to 50 cc. and used for the determination.—(W. P. S.; through *The Analyst*.)

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VANILLA EXTRACTS; DETERMINATION OF THE LEAD NUMBER OF —. H. J. Wichmann. *J. Ind. Eng. Chem.*, 1912, 13, 414-418.—The following procedure is recommended to obtain a maximum precipitation and to combine determinations of the lead value and alcohol content of vanilla extracts. A mixture of water, 175, 8 per cent. normal lead acetate solution, 25 and vanilla extract, 50 cc. is distilled; 200 cc. of distillate is collected and the alcohol content is calculated from the sp. gr. of the distillate. The residue in the distillation flask is diluted to 100 cc. with water free from carbon

dioxide, filtered, and 10 cc. of the filtrate is mixed with 25 cc. of water, 10 cc. of dilute sulphuric acid and 100 cc. of alcohol are added; the precipitated lead sulphate is collected and weighed. A control determination is made at the same time, using water containing 5 drops of glacial acetic acid in place of the vanilla extract. The quantity of lead precipitated by the extract and expressed as g. per 100 cc. is the lead value; for genuine undiluted extracts it is not less than 0.55. Sugar, glycerol, and coumarin do not interfere with the determination; if added vanillin is present it must be removed by extracting 50 cc. of the sample with three successive quantities of 50 cc. of a mixture of equal vols. of ether and petroleum spirit; the extracted aqueous solution is then used for the determination.—(W. P. S.; through *The Analyst.*)

ALCOHOL AS LOCOMOTIVE FUEL IN BRAZIL.—Consul C. R. Cameron of Pernambuco, reports that there are in his district approximately eighty modern cane-sugar factories, which have about 800 miles of railway, of from 0.75 to 1 meter gauge, operated at present by wood-burning locomotives. The fuel problem, however, is becoming a serious one and as a result the sugar-mill operators are turning their attention to the matter of reducing wood consumption and the substitutes. Consequently great interest is being shown in the substitution of alcohol, which is produced in large quantities on the sugar plantations from the molasses finals. Pernambuco has recently adopted the use of alcohol to which 5 per cent. gasoline has been added as an automobile fuel (see *Commerce Reports*, Mar. 15, 1921). The manufacturers are, therefore, naturally interested in using their own inexpensive product for their railways. The current price of alcohol is about \$0.22 per gallon, but the cost to the producer is much less. It is suggested that American manufacturers of locomotives capable of burning alcohol communicate with the Pernambuco sugar mills, a list of which may be obtained from the Latin-American Division of the Bureau of Foreign and Domestic Commerce or from any of the district or co-operative offices by referring to File No. L. A. 12012.—(Through *Commerce Reports*.)

FORMALDEHYDE AND PARAFORMALDEHYDE; DETERMINATION OF —IN TABLETS. N. Evers and C. M. Caines. Brit. Pharm. Conf., June, 1921. *Pharm. J.*, 1921, 470.—A tablet is weighed, boiled with

200 cc. of water for 30 mins. under a reflux condenser, the solution cooled, diluted to 500 cc. and filtered. Ten cc. of the filtrate is placed in a test-tube and a series of standards is prepared in 10 test-tubes, these containing, respectively, quantities of 0.1 to 1.0 cc. of 0.0038 per cent. formaldehyde solution, and each diluted to a volume of 10 cc. To each tube is added 2 cc. of Schiff's reagent and the colorations obtained are compared after the lapse of 3 mins. The presence of lactose, sucrose, and menthol does not interfere.—(W. P. S.; through *The Analyst*.)

ESTIMATION OF SANTONIN IN WORMSEED.—Kariyone and Kimura recommend the following method for the assay of wormseed: 10 gm. of powdered wormseed is extracted with ether for three hours in a Soxhlet extractor. The ether is removed by evaporation, and the residue boiled for thirty minutes, under a reflux condenser, with 100 cc. of barium hydroxide solution (5 per cent.). The solution, after being saturated with carbon dioxide until it turns blue litmus red, is then filtered. Eighty cc. of the filtrate (=8 gm. of drug) is placed in a separator of 200 cc. capacity; 10 cc. of hydrochloric acid (15 per cent.) and 20 cc. of chloroform are added, and the mixture is vigorously shaken for two minutes. After standing for a few minutes the clear chloroformic solution is filtered through a filter, previously moistened with chloroform, into a flask of 200 cc. capacity. The acid solution is then shaken three times, using on each occasion 10 cc. of chloroform, each washing being filtered through the same filter. The total chloroformic solution is evaporated to dryness, and the residue dissolved in 30 cc. of hot alcohol. After cooling, the alcoholic solution is neutralized with N/10 solution of potassium hydroxide, using phenolphthalein as indicator. Thereupon 20 cc. of N/10 solution of potassium hydroxide is further added, and the mixture boiled for thirty minutes under a reflux condenser. After cooling, it is re-titrated with N/10 hydrochloric acid. On the other hand, 30 cc. of the alcohol used to dissolve the chloroformic extract is treated with 20 cc. of N/10 solution of potassium hydroxide in the same way as described above, and neutralized with N/10 hydrochloric acid. If the number of cc. of N/10 hydrochloric acid used in the first instance is =X, and in the second test =Y, the percentage of santonin present is calculated by the use of the following formula:

$$\text{Percentage of santonin} = \frac{(Y-X) \times 2.462}{8}$$

This method was found to be superior to that of Katz, particularly in the presence of small amounts of santonin.—(Through *The Pharm. Jour. and Pharm.*)

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ISO-ALCOHOLIC ELIXIR.—With the object of using a minimum amount of alcohol so as to produce an elixir of an alcoholic strength, just sufficient to dissolve the medicament of which it is the vehicle, Dr. Bernard Fantus and Mr. C. M. Snow have devised the following formula:

Compound spirit of orange .....	10
Syrup .....	375
Purified talc .....	30
Alcohol .....	50
Glycerin .....	200
Distilled water to make .....	1,000

Mix the compound spirit of orange with the alcohol. Add the glycerin, syrup, and then the water, each of these in several portions, agitating after each addition. Mix the purified talc intimately with the liquid, and then filter through a wetted filter, returning the first portion of the filtrate until a transparent liquid is obtained.

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## NEWS ITEMS AND PERSONAL NOTES

SCIENTIFIC BODY HONORS PHARMACIST EXPLORER.—The American Pharmaceutical Association assembled for its annual meeting at New Orleans has shown its respect and high esteem for one of its leading members, Dr. Henry H. Rusby, Dean of the College of Pharmacy, Columbia University. Doctor Rusby is now in the interior of Bolivia, La Paz, directing the work of the Mulford Exploration. His object is the search for new drugs and medicinal plants together with botanical and zoological specimens of all kinds.

Doctor Rusby is no longer a young man and his boldness in undertaking a tropical exploration of this kind is hailed by his friends as one of the heroic phases of modern pharmaceutical and botanical science.

By unanimous vote the following message was cabled to Doctor Rusby:

"The American Pharmaceutical Association in convention assembled at New Orleans September 8, 1921, sends hearty greetings to Prof. Henry H. Rusby, and wishes him a successful consummation on his exploration trip and a safe return therefrom."

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AMBROSE HUNSMERGER, THE NEW PRESIDENT OF THE N. A. R. D.—The good wishes of this Journal are herewith conveyed to the new president of the National Association of Retail Druggists. A real pharmacist, ever interested in the welfare of his profession and willing to work in its interest, Mr. Hunsberger well deserves this additional honor which has come to him. The Association which has so honored him is to be congratulated upon engaging the services of so valuable and constructive a leader.

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MERCK'S NEW REAGENT CATALOG AND PRICE LIST.—Merck & Co. are distributing a new edition of their booklet *Blue Label Reagents and Other Laboratory Chemicals*. Merck's Blue Label Reagents, familiarly known as M. B. L., are made according to the requirements in *Standards and Tests for Reagent Chemicals*, published in 1920 by D. Van Nostrand & Co., of New York, and a special feature of the new catalog is the concise summary under each reagent showing its standard of purity, methods of testing, and other data taken from that textbook with the author's permission. Such of Merck's "White Label" chemicals of H. P., "C. P." and other grades as are of particular interest to laboratory workers are also listed and current prices are given throughout. The booklet, therefore, should be of interest to chemists generally as a manual and price list.

Copies may be obtained by addressing Merck & Co., 45 Park Place, New York.

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PENNSYLVANIA STATE MEDICAL SOCIETY MEETING.—One of the features of the Pennsylvania State Medical Society meeting, held in Philadelphia during the week of October 3, was a visitation to the Mulford Biological Laboratories, at Glenolden, Pa., which is just nine miles outside of the city.

A large number of the members, with their wives and friends, took advantage of this opportunity to view the largest biological laboratories in this country, if not in the world, to see how anti-toxins, vaccines, serobacterins, etc., are made, and to see many of the actual operations, such as injecting and bleeding of horses, etc.

Special trains had been provided by the H. K. Mulford Company for conveying the visitors to and from the laboratories. Refreshments were served on the grounds, and there was a barn dance for the amusement of those who were not particularly interested in the scientific work.

A feature which attracted special attention was the parade of immunized horses, in which these handsome and noble beasts passed proudly in review, as though conscious of the great service they are rendering to humanity.

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## BOOK REVIEWS

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OSMOTISCHE UNTERSUCHUNGEN. Studien zur Zellmechanik von Dr. W. Pfeffer. Second, unchanged edition, with five woodcuts. Leipzig, William Englemann.

Dr. Pfeffer was Professor of Botany in Basel when he undertook a series of investigations into the phenomena of osmosis, the results of which proved one of the most important phases in the development of physical chemistry. The volume in hand is a reprint of his work, published in 1876, issued as a memorial of the author, who died in January, 1920. The history of the subject shows, as usual in science, a very early anticipation of the general features of the investigation, Pfeffer giving in his book a summary of the data. As early as 1748, the Abbé Nollet noted osmotic action, but his work attracted so little attention that a later investigator, Fischer, was considered by many as the discoverer. In the second quarter of the nineteenth century, Dutrochet made investigations and introduced the terms "endosmose" and "exosmose" for the respective movements of currents in and out of the cell. As far as nationalistic feelings are concerned, the honors appear, indeed, to be fairly easy; the names of Pfeffer, Dutrochet and Graham being about equally prominent in the early history. Graham's early results in

1854 were of great importance, leading to the introduction of the terms "crystallloid" and "colloid" and to the process of dialysis. "Colloid chemistry" has become a most important branch of the science.

It is interesting to note that Pfeffer was a botanist, and that his studies were determined by his interest in the physiology of the living cell. It was Pfeffer who made the ingenious improvement by which the membrane was able to sustain a high pressure. The highest osmotic pressure will be obtained when the membrane is permeable by the dissolving medium (solvent) and not by the dissolved substance (solute). Pfeffer employed a porous cup in the walls of which copper ferrocyanide was produced by the diffusion of copper sulphate and potassium ferrocyanide from opposite sides. This pot was connected with a manometer tube. Naturally, this early apparatus was not entirely satisfactory, and improvements have been made so to secure greater accuracy, yet Pfeffer's results remained for a long time the principal data, being indeed, the only quantitative measurements, and produced a deep effect on the history of the chemistry and physics of solutions.

The publisher presents in the present volume, as already noted, an exact reprint of the original work, which appeared in 1876, except addition of a note by Dr. F. Czapek. Reference is made in this introduction to the important additions to the knowledge of the physical chemistry of solution by H. N. Morse and his co-workers in the laboratory of the Johns Hopkins University. An account of these investigations appeared in pamphlet form in 1914, under the title of "The Osmotic Pressure of Aqueous Solutions." The extensive studies since made in this field are familiar to physical chemists.

The book itself is well printed and is an interesting contribution to the classics of chemistry. Physical chemical phenomena received but scant notice in the manuals of physics or chemistry in the days when Dutrochet, Graham, Pfeffer and many others were working, and the topic first made its appearance in manual of chemistry as "chemical physics," but now it forms the subject of independent manuals and has a large part in the literature of the science.

The firm of Wilhelm Englemann deserves the thanks of chemists for re-issuing this important and interesting contribution, the

original addition having been long out of print. The price of the book is given as 32 marks, bound, with the usual note of high percentage increase under the rulings of the trade union, but in view of the changing value of the mark the price to the American buyer is uncertain.

HENRY LEFFMAN.

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A TEXTBOOK OF ORGANIC CHEMISTRY. By JOSEPH S. CHAMBERLAIN, Ph. D., Professor of Organic Chemistry, Massachusetts Agricultural College. P. Blakiston's Sons and Company, Philadelphia. \$4 net.

This work of 927 pages is an attempt on the part of the author "to present the subject (of organic chemistry) in a sufficiently elementary manner so as not to be beyond the grasp of the student in his first course in organic chemistry, yet, at the same time to make the book comprehensive in that it takes up the entire field by taking up practically all of the important groups of compounds." "The book is written primarily as a textbook for the undergraduate student and the instructor," but, in the opinion of the reviewer, the author has reason for his hope "that those who have already studied the subject may find it of value for its general presentation."

It is written in more or less of free lecture style, in language that is easily understood. There is some repetition of steps involved in reactions but all is to the advantage of the reader. In this sense it may be considered elementary, but when one notes the very large number of classes of compounds and individual compounds that are mentioned he must admit that in this sense the book is far from elementary.

A careful reading of the most of the text discloses but very few errors, something which cannot be said truthfully of many new works. Paper and typography are good. In addition to 31 pages, in double column, of index, there are 35 pages devoted to a survey of contents.

The reviewer knows of no recent book which he would more earnestly recommend to students in schools, and others who wish a good general survey of the field of organic chemistry.

F. P. S.

ORGANIC COMPOUNDS OF MERCURY. By FRANK C. WHITMORE, Ph. D. 397 pages. The Chemical Catalogue Company, Inc., New York. Price, \$4.50.

This book is the third of a series of monographs to be issued by the American Chemical Society on subjects of current interest, written by persons who are considered authorities on their respective subjects. The purpose of these monographs is to present the available knowledge on the chosen subject in readable form and to promote research in the branch of science concerned in each particular subject.

This particular book is claimed to be the only one in any language on this subject. Not all organic compounds which contain mercury are considered, the book treating almost solely of the true organic compounds of mercury in which the element is attached directly to carbon. Compounds of mercury not discussed in the text are made available for study by the supplementary bibliographical lists in the Appendix.

The arrangement of compounds is such as serves the general chemist who wishes to know what has been done in the field as a whole, as well as the specialist who wishes to learn quickly what has been done in any particular portion of the field.

The subject matter is divided into fourteen chapters covering 345 pages, and treats of General Methods of Preparation and General Properties and Reactions of Organic Mercury Compounds, and Mercury Derivatives of the various classes of Organic Compounds.

Five appendices take up Analysis of Organic Mercury Compounds, List of Proprietary Mercurials, an extensive Bibliography of Biological and Pharmacological Work with Organic Mercury Compounds, List of Patents dealing with Organic Mercury Compounds. Finally, there is a good subject index as well as an author index.

F. P. S.